| | | |
|---|---|---|
| PI: **Gifford, Rene H** | Title: Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy | |
| Received: 08/16/2018 | FOA: PA18-334<br>Clinical Trial:Required | Council: 01/2019 |
| Competition ID: FORMS-E | FOA Title: NIDCD Clinical Trials in Communication Disorders (R01-Clinical Trial Required) | |
| **1 R01 DC017683-01A1** | Dual: | Accession Number: 4206008 |
| IPF: 10040927 | Organization: VANDERBILT UNIVERSITY MEDICAL CENTER | |
| Former Number: | Department: Hearing And Speech Sciences | |
| IRG/SRG: LCOM | AIDS: N | Expedited: N |
| Subtotal Direct Costs<br>(excludes consortium F&A)<br>Year 1: [redacted]<br>Year 2: [redacted]<br>Year 3: [redacted]<br>Year 4: [redacted]<br>Year 5: [redacted] | Animals: N<br>Humans: Y<br>Clinical Trial: Y<br>Current HS Code: 30<br>HESC: N | New Investigator: N<br>Early Stage Investigator: N |
| | | |
| *Senior/Key Personnel:* | *Organization:* | *Role Category:* |
| Rene Gifford | Vanderbilt University Medical Center | PD/PI |
| Stephen Camarata | Vanderbilt University Medical Center | MPI |
| Robert Labadie | Vanderbilt University Medical Center | Other (Specify)-Co-Investigator |
| Jack Noble | Vanderbilt University | Other (Specify)-Co-Investigator |
| Benoit Dawant | Vanderbilt University | Other (Specify)-Co-Investigator |
| Mary Dietrich | Vanderbilt University | Other (Specify)-Co-Investigator |
| Susan Nittrouer | University of Florida | Other (Specify)-Consultant |
| Ferenc Bunta | The University of Houston | Other (Specify)-Consultant |

OMB Number 4040-0001
Expiration Date 10/31/2019

APPLICATION FOR FEDERAL ASSISTANCE
**SF 424 (R&R)**

| 3. DATE RECEIVED BY STATE | State Application Identifier |
|---|---|
| | [redacted] |

**1. TYPE OF SUBMISSION***

❍ Pre-application ● Application ❍ Changed/Corrected Application

**4.a. Federal Identifier**
DC017683

**b. Agency Routing Number**

**2. DATE SUBMITTED**
2018-08-16

**Application Identifier**
M0050027

**c. Previous Grants.gov Tracking Number**

**5. APPLICANT INFORMATION** **Organizational DUNS*:** [redacted]

Legal Name*: Vanderbilt University Medical Center
Department: Hearing And Speech Sciences
Division: School of Medicine
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]

Person to be contacted on matters involving this application
Prefix: First Name*: Donald Middle Name: Clinton Last Name*: Brown Suffix:
Position/Title: Director, Office of Sponsored Programs
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email [redacted]

**6. EMPLOYER IDENTIFICATION NUMBER** *(EIN) or (TIN)** [redacted]

**7. TYPE OF APPLICANT*** M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
**Small Business Organization Type** ❍ Women Owned ❍ Socially and Economically Disadvantaged

**8. TYPE OF APPLICATION***

❍ New ● Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

**Is this application being submitted to other agencies?*** ❍Yes ●No What other Agencies?

**9. NAME OF FEDERAL AGENCY***
National Institute on Deafness and Other Communication Disor

**10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER**
TITLE: NIDCD Clinical Trials in Communication Disorders (R01-Clinical Trial Required)

**11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT***
Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy

**12. PROPOSED PROJECT**
Start Date* Ending Date*
04/01/2019 03/31/2024

**13. CONGRESSIONAL DISTRICTS OF APPLICANT**
[redacted]

# SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE



**14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION**

Prefix: First Name*: Rene Middle Name: H Last Name*: Gifford Suffix:

Position/Title: Professor
Organization Name*: Vanderbilt University Medical Center
Department: Hearing And Speech Sciences
Division: School of Medicine
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email*: [redacted]

**15. ESTIMATED PROJECT FUNDING**

a. Total Federal Funds Requested* [redacted]
b. Total Non-Federal Funds* [redacted]
c. Total Federal & Non-Federal Funds* [redacted]
d. Estimated Program Income* [redacted]

**16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?***

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

**17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)**

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

**18. SFLLL or OTHER EXPLANATORY DOCUMENTATION** File Name:

**19. AUTHORIZED REPRESENTATIVE**

Prefix: First Name*: Donald Middle Name: Clinton Last Name*: Brown Suffix:

Position/Title*: Director, Office of Sponsored Programs
Organization Name*: Vanderbilt University Medical Center
Department: Office of Sponsored Programs
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email*: [redacted]

**Signature of Authorized Representative***
Brown,Donald Clinton

**Date Signed***
08/16/2018

**20. PRE-APPLICATION** File Name:

**21. COVER LETTER ATTACHMENT** File Name:M-13_RRSF424_Cover_Letter.pdf

# 424 R&R and PHS-398 Specific
# Table Of Contents

SF 424 R&R Cover Page....1
Table of Contents....3
Performance Sites....4
Research & Related Other Project Information....5
Project Summary/Abstract(Description)....6
Project Narrative....7
Facilities & Other Resources....8
Equipment....10
Research & Related Senior/Key Person....12
Research & Related Budget Year - 1....56
Research & Related Budget Year - 2....59
Research & Related Budget Year - 3....62
Research & Related Budget Year - 4....65
Research & Related Budget Year - 5....68
Budget Justification....71
Research & Related Cumulative Budget....74
Research & Related Budget - Consortium Budget (Subaward 1)....75
Total Direct Costs Less Consortium F&A....92
PHS398 Cover Page Supplement....93
PHS 398 Research Plan....95
Introduction to Application....96
Specific Aims....97
Research Strategy....98
PHS Human Subjects and Clinical Trials Information....110
Study 1: Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, Literacy....112
Inclusion Enrollment Reports....119
Multiple PD/PI Leadership Plan....134
Bibliography & References Cited....135
Consortium/Contractual Arrangements....143
Letters of Support....145
Resource Sharing Plan(s)....147

OMB Number: 4040-0010
Expiration Date: 10/31/2019

# Project/Performance Site Location(s)

**Project/Performance Site Primary Location**

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Vanderbilt University Medical Center
Duns Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

**Project/Performance Site Location 1**

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Vanderbilt University
DUNS Number: [redacted]
Street1*: [redacted]
Street2: [redacted]
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

**Additional Location(s)** File Name:





Funding Opportunity Number: PA-18-334. Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED Other Project Information

**1. Are Human Subjects Involved?*** ● **Yes** ❍ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ❍ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ● **Yes** ❍ **No**

IRB Approval Date:

Human Subject Assurance Number 00005756

**2. Are Vertebrate Animals Used?*** ❍ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ❍ Yes ❍ No

IACUC Approval Date:

Animal Welfare Assurance Number

**3. Is proprietary/privileged information included in the application?*** ❍ **Yes** ● **No**

**4.a. Does this project have an actual or potential impact - positive or negative - on the environment?*** ❍ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ❍ Yes ❍ No

4.d. If yes, please explain:

**5. Is the research performance site designated, or eligible to be designated, as a historic place?*** ❍ **Yes** ● **No**

5.a. If yes, please explain:

**6. Does this project involve activities outside the United States or partnership with international collaborators?*** ❍ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

| | Filename |
|---|---|
| **7. Project Summary/Abstract*** | M-5_Project_Summary.pdf |
| **8. Project Narrative*** | M-1_Narrative.pdf |
| **9. Bibliography & References Cited** | M-4_Bibliography.pdf |
| **10.Facilities & Other Resources** | M-2_Facilities.pdf |
| **11.Equipment** | M-3_Equipment.pdf |





Funding Opportunity Number: PA-18-334. Received Date: 2018-08-16T11:14:30.000-04:00

## PROJECT SUMMARY

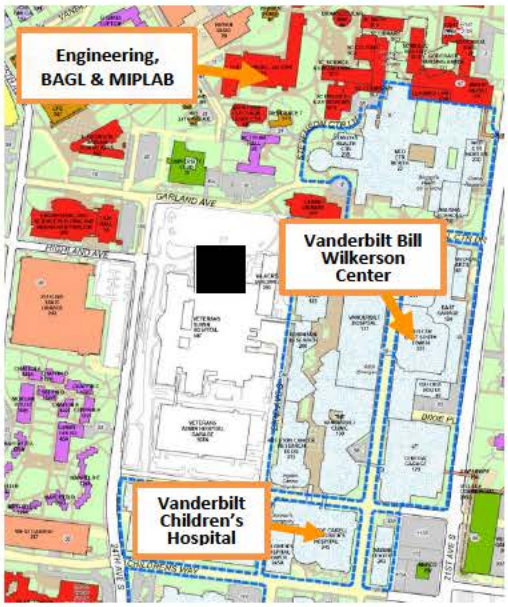
Although the recent literature has indicated that children receiving cochlear implants (CIs) often have dramatically improved speech and language ability relative to previous generations of children with hearing loss, many pediatric CI recipients display persistent speech and language disorders despite early implantation and associated speech/language intervention. There is a striking paucity and ongoing need for studies that systematically examine the relationship between intracochlear electrode location, audiological profile, and subsequent phonological awareness, speech, language, and literacy in pediatric CI recipients. This project provides a unique opportunity to examine whether individualized, ***image-guided CI programming (IGCIP)*** significantly improves outcomes in pediatric CI patients. The proposed research activities will examine the impact of personalized IGCIP in pediatric CI recipients on measures of basic auditory function (spectral, temporal, and spectrotemporal resolution), word and non-word recognition, speech production, language, phonological awareness, and reading comprehension using a double blind, waitlist control randomized clinical trial (RCT) design. A total sample of 72 children with CIs aged six to twelve years old will be enrolled in the project: half (n = 36) will be randomized to an immediate IGCIP condition and half to a waitlist control condition. The waitlisted participants (n = 36) will undergo IGCIP after 12 months of monitoring and then followed for an additional 12 months after intervention (total time in the study for both groups: 24 months). Those immediately provided with IGCIP will also be followed for a total of 24 months. All participants will undergo extensive audiological assessment as well as tests of phonological awareness, speech, language, and literacy at baseline as well as at regular intervals: 2, 6, 12, 14, 18, and 24 months. We will use predictor analyses to determine the impact of immediate and deferred IGCIP on subsequent auditory, speech, language, and literacy outcomes.

## PROJECT NARRATIVE

Despite significant advancements in technology and outcomes, pediatric cochlear implant (CI) recipients display persistent delay on measures of speech, language, and literacy despite early implantation and extensive speech/language intervention. Most CI recipients are programmed using a one-size-fits-all approach to setting upper and lower stimulation levels, maximum number of active electrical contacts, and selection of various signal processing parameters for electrical stimulation of the auditory system. Our interdisciplinary research team will examine the impact of a personalized, image-guided approach to CI programming and its effect on auditory processing, speech recognition, speech production, phonological processing, language, and literacy.

## FACILITIES AND RESOURCES

**Vanderbilt University Medical Center and Vanderbilt University** are both ideally suited for the proposed project. The Vanderbilt Bill Wilkerson Center located on the Vanderbilt University Medical Center campus has a large cochlear implant program which has recently been estimated to be the third largest implant program in the United States. Over the past three years, Vanderbilt has been implanting approximately 250 patients each year and has implanted over 3000 patients since the inception of the program. Given that Vanderbilt University is located within a large metropolitan area, there are many implant recipients who live either within the immediately surrounding communities or within a driving distance. The Cochlear Implant program, research laboratories (described below), engineering building, and medical facilities are collocated on a single campus are all within walking distance. Secure and reliable data exchange is already in place between these building for other existing collaborations using high speed encrypted network tunnels. The two PI's (Drs. Gifford and Camarata) and the Co-I's (Drs. Dawant, Labadie, and Noble) have long a history of collaboration.




**Cochlear Implant Research Laboratory**
The Vanderbilt Cochlear Implant (CI) Research Laboratory, directed by PI Dr. Gifford, is a 475-ft$^2$ space equipped with two, single-walled sound booths. [redacted] All audiological and auditory psychophysical assessments will take place in [redacted] The Cochlear Implant Research Laboratory has all equipment needed to carry out the proposed research activities (see Equipment).

**Developmental Disabilities Laboratory**
The Developmental Disabilities Speech and Language Lab, directed by PI Dr. Camarata, [redacted] The Lab consists of two Assessment/Treatment/Recording rooms, one observation room, three computer workstations, and one storage room that includes speech-language and achievement tests (and test records). The assessment rooms are equipped with built-in digital audio and video recording equipment (see Equipment for additional detail).

**Biomedical Image Analysis for Image Guided Interventions Laboratory (BAGL)**
The BAGL laboratory, directed by Co-I Dr. Noble, is a 500-ft$^2$ space [redacted] The lab has open office space for multiple research assistants. Equipment is detailed on the equipment page.

**Medical-image Processing Laboratory**
The Medical Image Processing laboratory (MIPLAB), directed by Co-I, Dr. Dawant, is 600-ft$^2$ equipped with state of the art computers. Thanks to existing multi-institutional projects, all the IT infrastructure required to transfer and store patient data in an HIPAA compliant way is in place. [redacted] The MIPLAB has high speed connections to the Vanderbilt University Advanced Computing Center for Research and Education (see below) that will be used for tasks that require massive parallel computing and to the Vanderbilt Medical Center where images will be acquired [redacted]

**Computer Assisted Otologic Surgery Lab (CAOS)**
The CAOS Laboratory, directed by Co-I Dr. Labadie, consists of over 2000-ft$^2$ in three inter-connected rooms [redacted] Most relevant to the current proposal is the **portable flat-panel volumetric computers tomography (fpVCT) Xoran scanner** which is used to patients on site and/or in the operating room at the time of cochlear implant surgery.

**General Facilities Description:** The Department of Hearing and Speech Sciences comprises one part of the Vanderbilt Bill Wilkerson Center for Otolaryngology and Communication Sciences, which is housed within five

floors of a 10-story building on the campus of the Vanderbilt University Medical Center. [redacted] is dedicated to research and houses over 20 separate laboratories that conduct both clinical and basic investigations in the areas of hearing, speech, and language science. Emphasis is on both behavioral and electrophysiological measurements associated with communication science and communication disorders. The many ongoing research projects are tied closely to the academic program [redacted] and to the speech, language, and audiology clinics that serve the Middle Tennessee region [redacted]. Research activity is also coordinated with the Department of Otolaryngology and the Vanderbilt Voice and Balance Disorders clinics [redacted]. In addition, animal research facilities associated with communication science are located in other buildings on the Vanderbilt University Medical Center campus.

**Office**: The PI's each have a private office in which participant counseling can be completed—including consenting and counseling regarding study performance. Each office has a 5-drawer, lateral file cabinet in which hard copies of participant data will be locked when not in use.

**Other**: The Department of Hearing and Speech Sciences at Vanderbilt University has a dedicated grants manager who assists with grant submissions, progress reports, and basic accounting. In addition to personnel, the budget has allocated funds for a project manager to assist with all aspects of the research project including IRB submission and management, subject recruitment, data collection, data entry, subject payment, analysis, presentation, and travel management for out-of-town participants.

**Resources available to Vanderbilt investigators**:
Vanderbilt University, with collaboration from a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) is a secure, web-based application that is flexible enough to be used for a variety of types of research. REDCap provides an intuitive user interface that streamlines project development and improves data entry through real-time validation rules (with automated data type and range checks). REDCap also provides easy data manipulation (with audit trails for reporting, monitoring and querying patient records) and an automated export mechanism to common statistical packages (SPSS, SAS, STATA, R/S-Plus). All data for this project will be stored in a REDCap electronic database.

REDCap servers are housed in a local data center at Vanderbilt, and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is recommended to Vanderbilt researchers by both our Privacy Office and Institutional Review Board. REDCap has been disseminated for local use at more than 420 other academic/non-profit consortium partners in 48 countries. Vanderbilt leads the REDCap Consortium, which currently supports more than 40,900 studies and 54,900 research end-users. More information about the consortium and system security can be found at http://www.project-redcap.org/.

Vanderbilt University has also developed ROCKET (*Research Organization, Collaboration, and Knowledge Exchange Toolkit)* which is a web-based tool for sharing information and documents, allowing members of a workspace to collaborate more effectively and efficiently by building and sharing web pages. Starting with a blank slate, members can add and organize files, blocks of text, headers, dividers, lists (bulleted, numbered and checklists), images, and tables, as well as additional pages. By default, everything in the workspace is private and only accessible to its members. If information needs to be shared with a larger audience, one or more pages can be made public for a read-only view.

**Animal - N/A**

## EQUIPMENT

**Cochlear Implant Research Laboratory**: The laboratory director and PI, Dr. Gifford, has all of the major equipment needed to perform the necessary experimentation in the proposal. The PI has been provided with dedicated lab space at Vanderbilt University Medical Center which houses two, single-walled sound booths. Both booths have calibrated audiometers with insert earphones, bone oscillators and sound field speakers allowing for standard audiometric and speech perception testing. Both sound booths are also equipped with the REVITRONIX R-SPACE™ 8-loudspeaker sound system and a rack of equipment controlling the system including a CX168 8-channel amplifier, MOTU 8-channel audio interface enabled with firewire, high-speed USB ports, spectrum analyzer, oscilloscope, and power conditioner. Additionally in each booth there is a Sound Track LXT sound level meter with mic and preamp suspended from the ceiling that can be used for real-time calibration prior to and during experimentation. We have an additional sound level meter dedicated for earphone calibration in the lab. Both booths also have an affiliated iMac and PC from which digitized speech stimuli can be presented for standard clinical assessment of speech recognition performance [e.g., the minimum speech test battery (MSTB) for pre- and post-operative assessment of speech recognition]. The CI Research Laboratory also has an Audioscan Verifit system in her lab for real-ear verification of hearing aid settings as well as a GSI Tympstar Pro allowing for electrically evoked stapedial reflex threshold (ESRT) verification of CI upper stimulation levels and assessment of middle ear function. Finally the CI Research Lab has a dedicated Intelligent Hearing Systems (IHS) auditory evoked potential (AEP) system used for assessing acoustic evoked AEPs for adults and pediatric CI recipients with residual acoustic hearing.

**Developmental Disabilities Laboratory:** The Developmental Disabilities Laboratory director and PI, Dr. Camarata, includes 4 video and speech coding stations, two therapy/diagnostic rooms with state of the art video recording equipment, and four camcorders. The Lab equipment includes five PC desktop computers with Video Analysis and SALT suites, a Mac server, and networked printers. Computers are outfitted with Microsoft Office, EndNote, SPSS, SALT, WavPedal, Start/Stop, and video storage (on the Mac server).

**Biomedical Image Analysis for Image Guided Interventions Laboratory (BAGL):** The BAGL laboratory is equipped with state of the art computers. This includes 1 rack-mounted processing server, a 20 TB file server, 2 cloned oracle database servers, and high end personal computers for all lab personnel. All of these machines are on a private sub-network behind a secure firewalled gateway server. The lab also has access to cluster computing resources at ACCRE with 620 compute nodes.

**Medical Image Processing Laboratory:** The medical image processing laboratory is equipped with a state of the art computer lab. This includes 5 rack-mounted computer servers, a 5TB file server, 2 cloned Oracle data base servers, and 15 high end personal computers. All these machines are networked and data servers are in a secure location behind a firewall. All of these machines are on a private sub-network behind a secure firewalled gateway server.

**Computer Assisted Otologic Surgery Lab (CAOS) & CT Scanners:** The **main CAOS lab** contains two Polaris infrared position trackers (Northern Digital, Waterloo, Ontario, CA), a MicronTracker visible-light position tracker (Claron Technology Inc, Toronto, Ontario, CA), a XarTrax steerable laser system (Traxtal, Inc, Toronto, Canada), two robots—a Mitsubishi RV-3S (Mitsubishi Electric & Electronics USA, Inc., Cyprus, CA) and a Motoman YR-SV035 (Motoman, Inc., West Carrollton, OH), an Acu-Rite III, xyz positioning system (Acu-Rite Companies Inc., Jamestown, NY), two surgical stations with electric and pneumatic drills, surgical microscopes, and associated instrumentation, and three cubicle stations. The separate **machine shop** contains an Ameritech CNC Jr. Milling Machine (Brousard Enterprises Inc., Sante Fe Springs, CA), FARO Gage-Plus measuring system (FARO Technologies, INC., Atlanta, GA), Delta tabletop band saw (Delta Tools, Jackson, TN), Delta belt sander (Delta Tools, Jackson, TN), Wilton tabletop drill press (WMH Tool Group, Inc., Elgin, IL), tool cabinet, metal stock shelf, and workbenches. Within the third CAOS room is a **portable flat-panel volumetric computers tomography (fpVCT) scanner** which is used to scan patients onsite and/or in the operating room at the time of CI surgery. Additionally Vanderbilt imaging has three 64-slice multi-detector CT scanners, three 16-slice multi-detector scanners, and one flat panel, volumetric computerized tomography (fpVCT) scanner.

**Computers/Software**: The PIs both have an iMac and PC computer in their offices. In her laboratory, Dr. Gifford has 2 iMac and 2 PC computers each of which is equipped with Windows 7 (via Parallels for Mac),

Microsoft Office, MATLAB, Adobe Audition, SPSS, Sigma Plot 10.0, GraphPad Prism, R, and a number of additional software packages required for electronic data storage, analysis, and plotting. In his laboratory, Dr. Camarata has 6 computers for coding and analyses purposes.

In addition, all project assistants will be granted password access to the research server. All Vanderbilt faculty and staff have free access to REDCap (Research Electronic Data Capture). REDCap is a secure, web-based application for building and managing online databases (see *Protection of Human Subjects* for additional detail). Each of the study personnel will be provided with a secure ID that will grant access the password protected database that will be created for this project and used for data transmission to the centralized data repository developed and managed by Drs. Gifford, Camarata, and Dawant.

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Rene Middle Name H Last Name*: Gifford Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University Medical Center
Department: Hearing And Speech Sciences
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: Doctor of Philosophy Degree Year: 2003

Attach Biographical Sketch*: File Name: ID-0015550_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

PROFILE - Senior/Key Person

Prefix: First Name*: Stephen Middle Name M Last Name*: Camarata Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University Medical Center
Department: Hearing And Speech Sciences
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: Doctor of Philosophy Degree Year: 1984

Attach Biographical Sketch*: File Name: ID-0004983_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Robert Middle Name F Last Name*: Labadie Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University Medical Center
Department: Otolaryngology
Division: School of Medicine
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Co-Investigator

Degree Type: Medical Doctor Degree Year: 1996

Attach Biographical Sketch*: File Name: ID-0039546_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Jack Middle Name H Last Name*: Noble Suffix:

Position/Title*: Research Asst Professor
Organization Name*: Vanderbilt University
Department:
Division: Unknown
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Co-Investigator

Degree Type: Doctor of Philosophy Degree Year: 2011

Attach Biographical Sketch*: File Name: ID-38062_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Benoit Middle Name Last Name*: Dawant Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University
Department:
Division: Unknown
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number: [redacted]

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Co-Investigator

Degree Type: Doctor of Philosophy Degree Year: 1987

Attach Biographical Sketch*: File Name: ID-28036_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Mary Middle Name S Last Name*: Dietrich Suffix:

Position/Title*: Professor
Organization Name*: Vanderbilt University
Department:
Division: Unknown
Street1*: School of Nursing
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Co-Investigator

Degree Type: Doctor of Philosophy Degree Year: 1996

Attach Biographical Sketch*: File Name: ID-28682_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Susan Middle Name Last Name*: Nittrouer Suffix:

Position/Title*: Consultant
Organization Name*: University of Florida
Department:
Division: Unknown
Street1*: [redacted]
Street2:
City*:
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Consultant

Degree Type: Doctor of Philosophy Degree Year: 1985

Attach Biographical Sketch*: File Name: ID-39419_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Ferenc Middle Name Last Name*: Bunta Suffix:

Position/Title*: Consultant
Organization Name*: The University of Houston
Department:
Division: Unknown
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number:

E-Mail* [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Other (Specify) Other Project Role Category: Consultant

Degree Type: Doctor of Philosophy Degree Year: 2005

Attach Biographical Sketch*: File Name: ID-39417_BN-1_BIOSKETCH.pdf

Attach Current & Pending Support: File Name:



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: René H. Gifford

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Arizona State University, Tempe, AZ | B.S. | 1995 | Speech and Hearing |
| Vanderbilt University, Nashville, TN | M.S. | 1997 | Hearing and Speech |
| Arizona State University, Tempe, AZ | Ph.D. | 2003 | Psychoacoustics |
| Arizona State University, Tempe, AZ | Postdoc | 2006 | Speech perception, cochlear implant signal processing |

### A. Personal Statement

I am a hearing scientist; however, I began my professional career 20 years ago as a clinical audiologist and have maintained an active clinical practice as I see complex and difficult-to-manage patients in the Cochlear Implant (CI) Audiology clinic at the Vanderbilt Bill Wilkerson Center. My line of research focuses on the study of basic auditory processing, spatial hearing, and speech recognition for individuals utilizing electric and acoustic stimulation with cochlear implants and hearing aids. Ultimately my goal is to improve outcomes for adults and children with cochlear implants affording each recipient the opportunity to achieve his/her maximum potential for communication and auditory perception. As a clinician/scientist in an academic medical environment with an on-site OPTION school for children with hearing loss, I have first-hand knowledge of the clinical problems associated with hearing loss, cochlear implants, speech and/or language delay, and the need for evidence-based recommendations for intervention. The research activities outlined in this proposal have the potential to revolutionize clinical intervention using a precision medicine approach to aural (re)habilitation for children with CIs including CI programming, prescriptive speech/language intervention, and ultimately optimization of outcomes. As PI, co-PI, and co-I on current and past NIH-funded grants, I have had nearly two decades of experience working with CI recipients on studies of speech perception and psychophysical estimates of auditory processing. Furthermore, I have administered all proposed auditory experimental protocols to pediatric CI recipients in our preliminary studies documenting the feasibility of the proposed research activities. These clinical, academic, and research experiences afford me the opportunity to significantly contribute to the proposed research activities as PI. It is an honor to be an active part of this interdisciplinary research team and I look forward to helping achieve significant improvements in outcomes for all cochlear implant recipients.

### B. Positions and Honors

**Positions and Employment**

2002-2003 NIH Pre-doctoral Fellow (F31), Psychoacoustics Laboratory, Arizona State University
2004-2006 NIH Post-doctoral Fellow (F32), Cochlear Implant Research Laboratory, Arizona State University
2006-2010 Director, Cochlear Implant Program, Mayo Clinic Rochester
2008-2010 Assistant Professor, Mayo Clinic College of Medicine
2011- Director, Cochlear Implant Program, Vanderbilt Bill Wilkerson Center

2011-2014 Assistant Professor, Vanderbilt University, Department of Hearing and Speech Sciences, Department of Otolaryngology
2012- Member, Vanderbilt Kennedy Center for Research on Education and Human Development
2014-2017 Associate Professor, Vanderbilt University, Department of Hearing and Speech Sciences, Department of Otolaryngology
2014- Tier I Training Faculty, Vanderbilt Brain Institute
2017- Professor, Vanderbilt University, Department of Hearing and Speech Sciences, Department of Otolaryngology

**Honors**

1995 Summa Cum Laude, undergraduate graduation Arizona State University
1991-1995 Arizona State Regents Scholarship, all four years of undergraduate study
1997 Jay W. Sanders "Honors in Audiology" Award, Vanderbilt University
2003 Mentored Student Poster Award. American Auditory Society. The effect of age on nonlinear cochlear processing.
2004 Mentored Student Poster Award. American Auditory Society. Speech recognition in a modulated background and the relation to recovery from forward masking: comparison of younger and older threshold-matched listeners
2005-2007 NIH Loan Repayment Program Grant: Combined electric and acoustic hearing
2007 The Best of 2007 "Most thought provoking" research article awarded for "Gifford et al., (2007). Auditory function and speech understanding in listeners who qualify for EAS surgery. *Ear Hear*, 28(2), 114S-118S," The Hearing Journal, 2007.
2008 The Best of 2008 "Great for the Clinician" research article awarded for "Gifford et al. (2008). Speech Recognition Materials and Ceiling Effects: Considerations for Cochlear Implant Programs, *Audiol Neurotol*, 13, 193-205*,"* The Hearing Journal, 2008.
2008 The Best of 2008 "Most thought provoking" research article awarded for "Gifford et al. (2008). Hearing preservation surgery: Psychophysical estimates of cochlear damage in recipients of a short electrode array, *J Acoust Soc Am*, 124, 2164-2173*."* The Hearing Journal, 2008.
2009 The Best of 2009 "Most thought provoking" research article (Co-author) awarded for "Dorman et al. (2009). Word recognition following implantation of conventional and 10 mm Hybrid electrodes. *Audiol Neurotol*, 14:181-189." The Hearing Journal, 2009.
2015 Louis M. DiCarlo Award for Recent Clinical Achievement, American Speech-Language-Hearing Association (ASHA)
2015 Selected as 1 of 18 VUMC featured StoryCorps interviews with Ally Sisler-Dinwiddie, AuD for *Voices of the NIH community*. Interview recording archived at the American Folklife Center at the Library of Congress.
2016 Featured scientist, National Public Radio, Science Friday: *Breakthrough: Portraits of Women in Science—Hearing a Whole New World*, aired live September 9, 2016. Video documentary and recorded live broadcast available at http://www.sciencefriday.com/segments/breakthrough-hearing-a-whole-new-world/
2017 Vanderbilt University Chancellor's Award for Research; The Chancellor's Award recognizes excellence on the part of faculty for published research, scholarship, or creative expression.

**Grant Review**

2011-2016 NIH NIDCD, Ad Hoc Reviewer, Communication Disorders Review Committee (CDRC)
2012 NIH NIDCD, Ad Hoc Reviewer, Special Emphasis Panel, ZDC1 SRB-R (35)
2013 NIH NIDCD, Ad Hoc Reviewer, Special Emphasis Panel, ZDC1 SRB-K (12)
2016-2020 NIH NIDCD, Permanent member, Communication Disorders Review Committee (CDRC)
2018 Department of Defense, Congressionally Directed Medical Research Programs, Hearing Restoration Research Program

### C. Contribution to Science

(1) We have developed a novel way to program cochlear implants using pre- and post-operative CT scans to specify the relationship between the cochlear implant (CI) electrode array and the locations of the primary auditory neurons located within the modiolus. To date, we have applied this technique to 226 adult CI recipients

and 36 pediatric CI recipients. After using the new program for at least 1 month, 156 of the 226 adults (69.0%) and 28 of the 36 pediatric patients (77.8%) have chosen to keep the new map either due to statistically significant improvement in speech understanding and/or subjective improvement in sound quality that was deemed significant enough for them to abandon the maps they had been using for, on average, 4½ years. Select related publications and patent (a-e) are shown below. I have worked as a co-investigator and co-PI on these projects.

a. Noble JH, Gifford RH, Labadie RF, Dawant BM. (2012). Statistical shape model segmentation and frequency mapping of cochlear implant stimulation targets in CT. *Med Imag Comput Assist Interv.* 15 (Pt 2): 421-8. PMID: 23286076
b. Noble JH, Gifford RH*****, Hedley-Williams A, Sunderhaus L, Labadie RF, Dawant BM. (2014). Clinical evaluation of an image-guided cochlear implant programming strategy. *Audiol Neurotol*. 19(6):400-11. PMID: 25402603. *****co-first author
c. Noble JH, Labadie RF, Gifford RH, Dawant BM. (2013). Image-guidance enables new methods for customizing cochlear implant stimulation strategies. *IEEE Trans Neural Syst Rehabil Eng*. 21(5):820-9. PMID: 23529109
d. Noble JH, Hedley-Williams A, Sunderhaus L, Dawant B, Labadie RF, Camarata S, Gifford RH. (2016). Image-guided cochlear implant (CI) programming can improve hearing outcomes for pediatric CI recipients. *Otol Neurotol*. 37(2):e63-9. PMID: 26756157

(2) I have worked as the PI on nearly 15-years of NIH-funded research evaluating psychophysical processing related to combined electric and acoustic stimulation (EAS) with cochlear implantation. During my F32 funded postdoctoral fellowship, I defined basic auditory properties of low-frequency acoustic hearing in EAS patients which led to additional prospective studies examining i) the efficacy of hearing preservation (e-g), ii) the underlying mechanisms driving EAS benefit (e-g), and iii) the best practices for optimizing EAS outcomes in a clinical environment (h). Work that my lab has completed over the past decade has documented significant speech understanding benefit for listening in complex environments including diffuse noise, reverberation, and informational masking, significant improvements in auditory localization abilities, retention of binaural hearing cues helpful for spatial hearing and speech understanding in noise, as well as optimization of EAS parameters for clinical applicability.

e. Gifford RH, Dorman MF, Skarzynski H, Lorens A, Polak M, Driscoll CLW, Roland P, Buchman CA. (2013). Cochlear implantation with hearing preservation yields significant benefit for speech recognition in complex listening environments. *Ear Hear*, 34(4):413-25. PMID: 23446225
f. Gifford RH, Grantham DW, Sheffield SW, Davis TD, Dwyer R, Dorman MF. (2014). Localization and interaural time difference (ITD) thresholds for cochlear implant recipients with preserved acoustic hearing in the implanted ear. *Hear Res*, 312:28-37. PMID: 24607490
g. Loiselle LH, Dorman MF, Yost WA, Cook SJ, Gifford RH. (2016). Using ILD or ITD cues for sound source localization and speech understanding in a complex listening environment by bilateral and hearing-preservation cochlear-implant listeners. *J Speech Lang Hear Res.* 59(4):810-8. PMID: 27411035
h. Gifford RH, Davis TJ, Sunderhaus LW, Menapace C, Buck B, Crosson J, O'Neill L, Beiter A, Segel P. (2017). Combined electric and acoustic stimulation (EAS) with hearing preservation: effect of cochlear implant low-frequency cutoff on speech understanding and perceived listening difficulty. *Ear Hear*, 38(5): 539-553. PMID: 28301392

(3) As co-I or co-PI on various projects related to test design for assessing speech understanding and non-linguistic assessment of CI outcomes, we have provided clinicians and researchers with a direct translation of research-proven tasks into validated clinical tests. These clinical tests have the potential to guide clinical decision making regarding cochlear implant candidacy, ear selection, and postoperative programming of CI processors. Our validated speech perception measures are now included in the adult minimum speech test battery (MSTB) and pediatric MSTB (PMSTB), both of which outline best-practices protocols for clinical assessment of CI recipients in Audiology practice. Our work with assessment of speech perception in adults and children with cochlear implants as well as our clinical translation of a psychoacoustic measure of spectral resolution has resulted in the development of the AzBio sentence materials (i), BabyBio sentence materials (j), the Quick Spectral Modulation Detection (QSMD) test (k), and the Pediatric Minimum Speech Test Battery (PMSTB) (l).

i. Spahr AJ, Dorman MF, Litvak LL, Van Wie S, Gifford RH, Loizou PC, Loiselle LM, Oakes T, Cook S. (2012). Development and Validation of the AzBio Sentence Lists. *Ear Hear*. 33:112-7. PMID: 21829134

j. Spahr AJ, Dorman MF, Cook SJ, Loiselle L, Hayes C, Hedley-Williams A, Sunderhaus LW, DeJong MD, Gifford RH. (2014). Development and validation of the pediatric AzBio sentence test. *Ear Hear* 35(4):418-22. PMID: 24658601
k. Gifford RH, Hedley-Williams A, Spahr AJ. (2014). Clinical assessment of spectral modulation detection for adult cochlear implant recipients: a non-language based measure of performance outcomes. *Int J Audiol.* 53(3):159-64. PMID: 24456178
l. Uhler K, Warner-Czyz A, Gifford RH. (2017). Pediatric Minimum Speech Test Battery (PMSTB). *J Am Acad Audiol*. 28(3): 232-247. PMID: 28277214

(4) I have worked as PI along with a number of collaborating clinician/scientists in the scientific evaluation of current cochlear implant (CI) candidacy indications. Based on both retrospective and prospective, longitudinal studies, we have concluded that both adult and pediatric labeled indications for implantation are overly restrictive not allowing for potentially hundreds of thousands of individuals who are significantly affected by moderate-to-profound sensory hearing loss to take advantage of the communicative benefits afforded by cochlear implantation. This work has led to 1) two of the three FDA approved CI manufacturers to commence multi-center FDA approved clinical trials to define revised indications for adult CI candidacy and 2) the FDA to convene an Ear, Nose, and Throat Devices Panel Meeting to review current labeled indications for pediatric CI candidacy. Related publications (o-r) are as follows:

o. Gifford RH, Shallop JK, Peterson AM. (2008). Speech Recognition Materials and Ceiling Effects: Considerations for Cochlear Implant Programs. *Audiol Neurotol,* 13:193-205. PMID: 18212519
p. Gifford RH, Dorman MF, Skarzynski H, Lorens A, Polak M, Driscoll CLW, Roland P, Buchman CA. (2013). Cochlear implantation with hearing preservation yields significant benefit for speech recognition in complex listening environments. *Ear Hear*. 34(4):413-25. PMID: 23446225
q. Carlson MC, Sladen DP, Haynes DS, Driscoll CLW, DeJong MD, Sunderhaus LW, Hedley-Williams A, Rosenzweig EA, Davis TJ, Gifford RH. (2015). Evidence for the expansion of pediatric cochlear implant candidacy. *Otol Neurotol*. 36(1): 43-50. PMID: 25275867
r. Sladen DS, Gifford RH, Haynes DS, Kelsall D, Benson A, Lewis K, Zwolan T, Fu, QJ, Gantz B, Gilden J, Westerberg B, Gustin C, White L, Driscoll CL. (2017). Evaluation of a revised indication for determining adult cochlear implant candidacy. *Laryngoscope*. 127(10):2368-2374. PMID: 28233910

**Complete List of Published Work in MyBibliography (from over 85 peer-reviewed publications):**
http://www.ncbi.nlm.nih.gov/sites/myncbi/rene.gifford.1/bibliography/40425043/public/?sort=date&direction=ascending

**D. Research Support**

**Ongoing Support**

R01 DC009404 Gifford (PI) 2009-2020
Title: Cochlear implants: combined electric and binaural acoustic stimulation
Goal: The goal of this study is to determine the efficacy of binaural hearing preservation for speech recognition in complex listening environments, the spatial resolution in adult cochlear implant recipients, and describe the underlying auditory mechanisms driving this benefit associated with electric and acoustic stimulation (EAS).
Role: Principal Investigator
Overlap: There is no overlap with this grant and the current proposal. This grant focuses on underlying binaural hearing mechanisms driving auditory perceptual benefit for adults combining electric and acoustic stimulation (EAS).

R01 DC13117 Gifford (PI) 2013-2018
Title: Clinical application of spectral envelope perception: cochlear implant evaluation
Goal: The goal of this project is to conduct a prospective, longitudinal study of acoustic and electric spectral resolution and speech recognition performance in adult cochlear implant (CI) recipients.
Role: Principal Investigator
Note: This grant is currently in a no-cost extension year. At the completion of the no-cost extension year, we will have met the objectives of this R01 clinical tool grant; thus, we will not be seeking renewal.

R01 DC014037 Noble (PI) 2014-2019
Title: Image-guided cochlear implant programming techniques
Goal: The goal of this project is to develop and evaluate new image-guided cochlear implant programming strategies that use objective information acquired from clinical images to determine patient customized frequency, current steering, and current focusing settings that lead to better hearing outcomes.
Role: Co-Investigator
Overlap: There is no scientific overlap with this grant and the current proposal. Dr. Noble's project is specific to adult CI recipients and more specifically the investigation of objective auditory electrophysiologic correlates for image-guided programming techniques.

R01 DC014462 Dawant (PI) 2015-2020
Title: Computer-assisted, image-guided programming of cochlear implants
Goal: The goal of this project is to investigate the relationship between electrophysiologic and psychophysical responses to electric stimulation and objective estimates of the electrode-to-neuron interface obtained via pre- and post-operative imaging and to automate our image-guided approach to cochlear implant programming.
Role: Co-Investigator
Overlap: There is no scientific overlap with this grant and the current proposal. Dr. Dawant's project is focused on adult CI recipients, comparison between auditory psychophysical and objective measures, and automation of the IGCIP process.

**Completed Support**

R01 DC010821 Gifford (Co-PI) 2010-2015
Title: Cochlear Implant performance in Realistic Listening Environments
Goal: The goal of this study is to assess speech recognition performance for unilateral and bilateral implant recipients in both standard and simulated realistic test environments, with the goal of creating a decision matrix that links data that can be easily collected in the clinic, e.g., CNC scores in quiet and the amount of residual hearing, with data that cannot be collected in the clinic, i.e., performance data collected with multiple, spatially separated loudspeakers
Role: Co-Principal Investigator (MPI)

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Camarata, Stephen M.

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor of Hearing & Speech Sciences, Professor of Psychiatry, Associate Professor of Special Education, Peabody College

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| San Diego State University, San Diego, CA | B.A. | 1979 | Communication Disorders |
| San Diego State University, San Diego, CA | M.A. | 1981 | Communication Disorders |
| Purdue University, West Lafayette, IN | Ph.D. | 1984 | Audiology & Speech Science |
| University of Arizona, Tucson, AZ | Post Doc | 1984-85 | Speech Science |

A. Personal Statement

My expertise is in clinical research addressing the assessment and treatment of speech and language disorders in children with disabilities, including children with Hearing Loss, children with Down Syndrome, children with Autism Spectrum Disorders (ASD) and children with SLI. The work on children with hearing loss and on those with language disorders is of particular importance to the proposed research. This includes assessment and treatment of speech and language disorders in these children and Dr. Gifford and the other members of the research team and I have published a number of studies relating the measurement of speech and language skills in these children. This collaborative work includes a preliminary investigation of speech and language abilities in children with cochlear implants that serves as the basis for the pilot data supporting this application. In addition, the past five years, I've been collaborating with [redacted] projects examining fatigue in children with hearing loss. This research includes assessment of language and literacy in these children. Finally, my own research has been focused on primary and tertiary outcomes in children with speech and language disorders arising from diverse etiology that provides specific expertise on: A) assessing children with disabilities who may be difficult to test (e.g., Down Syndrome, ASD) and B) exploring the relationships between speech, language, and related abilities (such as literacy) in these groups. It is perhaps noteworthy that this work includes successful (and productive) interdisciplinary collaboration both within Vanderbilt [redacted] and across sites [redacted]

B. Positions and Honors

Positions and Employment

1979 - 1981 Teaching Assistant, Dept of Speech Pathology and Audiology, San Diego State University
1981 - 1982 Clinical Fellow, Purdue University Speech and Hearing Clinic
1982 - 1984 Teaching and Research Assistant, Dept of Audiology and Speech Sciences, Purdue University
1984 - 1985 Postdoctoral Fellow, Early Childhood Language Laboratory, Dept of Speech and Hearing Sciences, University of Arizona
1985 - 1988 Assistant Professor, Dept of Special Education & Communication Disorders, Pennsylvania State University

| | |
|---|---|
| 1988 - 1990 | Assistant Professor, Dept of Speech and Hearing Sciences, University of California, Santa Barbara |
| 1990 - 1994 | Assistant Professor, Dept of Speech and Hearing Sciences, Vanderbilt University School of Medicine |
| 1994 - 2002 | Associate Professor, Dept of Speech and Hearing Sciences, Vanderbilt University School of Medicine |
| 1996 - 2017 | Associate Professor, Dept of Special Education, Peabody College, Vanderbilt University |
| 1999 - 2002 | Acting Director, John F. Kennedy Center for Research on Human Development, Vanderbilt University |
| 2002 - 2004 | Deputy Director, John F. Kennedy Center for Research on Human Development, Vanderbilt University |
| 2004 - 2009 | Director, Research Program in Communication & Learning, John F. Kennedy Center for Research on Human Development, Vanderbilt University |
| 2002 - pres | Professor, Dept of Speech and Hearing Sciences and Dept of Psychiatry, Vanderbilt University School of Medicine |
| 2018-pres | Professor, Dept of Special Education, Peabody College, Vanderbilt University |

Honors and Awards

| | |
|---|---|
| 1979 | Graduated with high honors and distinction, San Diego State University |
| 1979 | Phi Kappa Phi |
| 1986 | Member of the Outstanding Young Men of America |
| 1987 | "Who's Who in American Universities and Colleges" |
| 1988 | “Who's Who Among Health Science Professionals" |
| 1991 | Appointed Research Investigator, John F. Kennedy Center for Research in Human Development |
| 1997 - 2001 | Chair of the Special Interest Division on Treatment Efficacy of the American-Speech-Language Hearing Association |
| 2001 | Distinguished Faculty Honoree, Vanderbilt University |
| 2007-2011 | Chartered member, NIH Study Section on Child Psychopathology/Developmental Disabilities (CPDD) |
| 2009-2011 | Chair, NIH Study Section on Child Psychopathology/Developmental Disabilities (CPDD) |
| 2017 | Chair, NIH Review Panel, Autism Centers for Excellence (ACE) |
| 2015-2019 | Chartered Member, NIH Study Section on Communication Disorders Research (CDRC) |
| 2010 | Fellow, American Speech-Language Hearing Association |
| 2012 | Glenwood Endowed Lecture, University of Alabama, Birmingham |
| 2014 | Distinguished Service Award, Autism Speaks |
| 2015-2016 | Member, Institute of Medicine (National Academy of Sciences) Panel on Speech and Language Disorders in Children. |
| 2016-2018 | Member, Institute of Medicine (National Academy of Sciences) Panel on Health Outcomes in Children with Disabilities |
| 2017 | Art Wheeler Studio Award for Outstanding Service to Vanderbilt Translational and Clinical Science Award (CTSA). Vanderbilt University School of Medicine. |

C. Contributions to Science

My research is focused on assessment and treatment of speech and language disorders in children with various disability typologies including Down Syndrome, specific language impairment, phonological disorder, and autism spectrum disorder. Contributions in these areas include foundational intervention studies testing the effectiveness of treatments designed to parallel enhance naturally occurring language input within the theoretical framework of the transactional model of development (e.g., Nelson, 1989; Sameroff, 1978).

1. A significant contribution especially relevant to the proposed research has been assessing speech and language disorders in children with hearing loss. This relatively recent addition to my research portfolio has indicated that recent advances in hearing technology (e.g., cochlear implants), has dramatically improved outcomes in these children from the severe range, to patterning more like children without hearing loss who have language disorders. The research also includes measuring subjective fatigue in these children Example publications from this contribution include:

    a. Camarata, S., Werfel, K., Davis, T., Hornsby, B. W., & Bess, F. H. (2018). Language Abilities, Phonological Awareness, Reading Skills, and Subjective Fatigue in School-Age Children With Mild to Moderate Hearing Loss. *Exceptional Children*, 0014402918773316.
    b. Hornsby, B. W., Werfel, K., Camarata, S., & Bess, F. H. (2014). Subjective Fatigue in Children With Hearing Loss: Some Preliminary Findings. *American Journal of Audiology*, *23*(1), 129-134.
    c. Bess, F. H., Gustafson, S. J., Corbett, B. A., Lambert, E. W., Camarata, S. M., & Hornsby, B. W. (2015). Salivary Cortisol Profiles of Children with Hearing Loss. *Ear and Hearing*.
    d. Noble JH[1], Hedley-Williams AJ, Sunderhaus L, Dawant BM, Labadie RF, Camarata SM, Gifford RH. (2016) Initial Results With Image-guided Cochlear Implant Programming in Children. *Otology and Neurotology,* Feb;37(2):e63-e69.

2. A significant contribution has been improving speech disorders in children with Down syndrome. Unlike other children with severe speech disorders, these children have significant lifelong challenges with not only articulation accuracy but also limitations in producing intelligible and comprehensible speech. Example publications from this contribution include:

    a. Camarata, S., Yoder, P., & Camarata, M. (2006). Simultaneous treatment of grammatical and speech-comprehensibility deficits in children with Down syndrome. Down Syndrome: Research and Practice, 11(1), 9-17. PMID: 17048805
    b. Yoder, P. J., Woynaroski, T., & Camarata, S. (2016). Measuring Speech Comprehensibility in Students with Down Syndrome. *Journal of Speech, Language, and Hearing Research*, *59*(3), 460-467.
    c. Camarata, S. (1993). The application of naturalistic conversation training to speech production in children with speech disabilities. Journal of Applied Behavior Analysis, 26(2), 173-182.
    d. Yoder, P. J., Camarata, S., & Woynaroski, T. (2016). Treating speech comprehensibility in students with Down syndrome. *Journal of Speech, Language, and Hearing Research*, *59*(3), 446-459.

3. There have been a series of papers examining assessment and treatment of language disorders (especially grammatical morphology) in SLI. This work has been a primary contributor to a recent meta-analysis showing that this approach has a large intervention effect size. We believe that the approach will be effective in CI as well if the Image Guided Mapping procedures are beneficial to children with hearing loss.

    a. Camarata, S., Nelson, K. E., & Camarata, M. (1994). A comparison of conversation based to imitation based procedures for training grammatical structures in specifically language impaired children. Journal of Speech and Hearing Research, 37, 1414-1423.
    b. Leonard, L., Camarata, S., Brown, B. & Camarata, M. (2008). The acquisition of tense and agreement in the speech of children with specific language impairment: Patterns of generalization through intervention. Journal of Speech-Language-Hearing Research, 51, 120-125. PMID: 18230859
    c. Davis, T. N., Lancaster, H. S., & Camarata, S. (2016). Expressive and receptive vocabulary learning in children with diverse disability typologies. *International Journal of Developmental Disabilities*, *62*(2), 77-88.
    d. McDaniel, J., Camarata, S., & Yoder, P. (2018). Comparing Auditory-Only and Audiovisual Word Learning for Children with Hearing Loss. *The Journal of Deaf Studies and Deaf Education*.

4. In addition, there have been a number of assessment and intervention studies on speech and language intervention and on multisensory processing in children with autism. These include:

a. Camarata, S. (2014). Early identification and early intervention in autism spectrum disorders: Accurate and effective? International Journal of Speech-Language Pathology, 2014; 16(1): 1–10.
b. Stevenson, R. A., Siemann, J. K., Schneider, B. C., Eberly, H. E., Woynaroski, T. G., Camarata, S. M., & Wallace, M. T. (2014). Multisensory Temporal Integration in Autism Spectrum Disorders. *Journal of Neuroscience*, 34(3), 691-697.
c. Raghavan, R., Camarata, S., White, K., Barbaresi, W., Parish, S., & Krahn, G. (2018). Population Health in Pediatric Speech and Language Disorders: Available Data Sources and a Research Agenda for the Field. *Journal of Speech, Language, and Hearing Research*, *61*(5), 1279-1291.
d. Koegel, R. L., Koegel, L. K., & Camarata, S. M. (2010). Definitions of empirically supported treatment. *Journal of autism and developmental disorders*, *40*(4), 516-517.

**Publication Metrics**
Google Scholar Publications: 92 Google Scholar Citation Index: 2,236.

Research Gate Profile https://www.researchgate.net/profile/Stephen_Camarata
Impact Score: 29.92, Cumulative Impact: 78.77

CV available on Lab Website: https://medschool.vanderbilt.edu/developmental-disabilities-lab/

**D. Other Support**

Ongoing Research Support

H325D140087 (Schuele) 04/30/2016-08/31/2019 1.20 calendar months
U.S. Department of Education
TRILL: Training Exemplary Pre-Doctoral Researchers in Language Literacy
The goal of this project is to prepare 6 pre-doctoral students to conduct language and literacy intervention research and prepare the next generation of speech-language pathologists.
Role: Co-Director

R324A160300 (Bess) 09/28/2016-06/30/2019 1.80 calendar months
IES
Measurement of Listening Fatigue in School-Age Children with Disabilities
Goal: We plan to construct and validate a child-centered measure of listening fatigue for children with hearing loss (CHL) and other communication-based disabilities (CHLCD).
Role: Co-PI/PD

5UL1T$002243-02 (Bernard) 06/01/2017-02/28/2022 0.30 calendar months
NIH/NCATS
Vanderbilt Institute for Clinical and Translational Research (VICTR)
The major goal is to assist institutions to create a “novel, and integrative academic home for clinical and translational science.”
Role: Team Science Lead

N/A (Camarata, PI) 01/01/2014-12/31/2018 0.60 calendar months
[redacted]
Role: PI

Completed Research Support

R324A100225 (Yoder, PI) 09/01/2010-08/31/2015 1.20 Calendar Months
IES
Efficacy of Broad Target Speech Recasts on Students with Down Syndrome
The major goals of this project are to conduct an efficacy trial to determine whether broad target speech recasts significantly improves generalized speech comprehensibility in the connected speech of elementary school students with Down syndrome.
Role: Co-Investigator

R324A090181 (Kaiser, PI) 07/01/2009-06/30/2015 1.20 calendar months
IES
NCSER-EIECE G3: An Efficacy Trial of Enhanced Milieu Teaching Language Intervention with Language Delayed Toddlers
The specific aim of this proposed project is to determine whether language deficits can be prevented through early intervention in preschool children at high risk for persistent language delays.
Role: Co-Investigator

R324A110266 (Bess) 07/01/2011-06/30/2016 0.60 calendar months
IES
Fatigue and Listening Effort in School-Age Children with Hearing Loss
The major goals of this project are to examine whether school-age children with mild to moderate hearing loss expend greater listening effort and subsequently experience more fatigue under noise conditions (similar to a classroom) than a group of normal hearing children.
Role: Co-PD/PI

N/A (Camarata) 12/01/2011-12/31/2015 0.36 calendar months
[redacted]

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contr butors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

| NAME | POSITION TITLE |
|---|---|
| Labadie, Robert F. | Professor (with tenure) of Otolaryngology<br>Professor of Biomedical Engineering<br>Vanderbilt University, Nashville, TN |
| eRA COMMONS USER NAME<br>[redacted] | |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| University of Notre Dame, Notre Dame, IN | B.S. | 1988 | Mechanical Engineering |
| University of Pittsburgh, Pittsburgh, PA | Ph.D. | 1995 | Bioengineering |
| University of Pittsburgh, Pittsburgh, PA | M.D. | 1996 | Medicine |
| University of NC at Chapel Hill, Chapel Hill, NC | Residency | 1996-01 | Otolaryngology |
| Vanderbilt University-Owen School of Management | M.S. | 2012-13 | Management |

### A. Personal Statement

Over the past 16 years, I have been the clinical director of a multi-disciplinary research team composed of engineers, surgeons, audiologists, and biostatisticians which has focused on the use of image guidance techniques in the field of otology. This has included multiple NIH-funded endeavors in which I have served as PI including development of robotic techniques for surgically approaching the lateral skull base (R21EB006044–02) as well as development, clinical testing, and implementation of novel minimally-invasive surgical approaches for cochlear implantation (R01DC008408, R01DC010184). More recently our work has included use of imaging to improve cochlear implant programming and currently supported by two grants for which I am a co-I (R01DC014037, R01DC014462). Our compendium of work has expanded to include neuroscientists and speech language pathologists, and we now find ourselves in the unique situation to propose investigation of personalized algorithms for pediatric cochlear implant recipients. Given my experience leading multi-disciplinary teams and expertise in both surgery and engineering, I am happy to serve as Co-I lending my surgical and engineering expertise to this project investigating auditory, speech, language, and literacy outcomes following individualized programming for pediatric cochlear implant users. As an active clinician/scientist, I am acutely aware of the clinical problems associated with patient counseling and prognostic indecision due to highly variable outcomes for cochlear implant recipients—particularly pediatric cochlear implant recipients given the critical period for speech, language, and literacy. There are few interventions that are using a one-size-fits-all approach to rehabilitation. We have demonstrated in both adult and pediatric cochlear implant recipients that an individualized approach to otologic and audiologic rehabilitation results in statistical significant improvement in auditory-based outcomes. We have much to learn from this project with the ultimate goal of maximizing the potential of all implant recipients and I look forward to this collaborative project.

### B. Positions and Honors.

1996-1997 General Surgery Intern; University of North Carolina Hospitals
1997-2001 Otolaryngology Resident; University of North Carolina Hospitals
7/1/2001-6/30/2007 Assistant Professor; Vanderbilt University
Department of Otolaryngology-Head and Neck Surgery
Joint Appointment – Department of Biomedical Engineering
7/1/2007-12/31/2012 Tenured Associate Professor, Vanderbilt University
2011 – present Vanderbilt Institute in Surgery and Engineering (VISE), Steering Committee
09/2012-05/2014 Director of Research, Department of Otolaryngology-Head and Neck Surgery
06/2014-present Vice Chair, Chief Research Officer, Dept. Otolaryngology-Head and Neck Surgery
1/1/13 – present Tenured Professor, Vanderbilt University
2/1/15 – 5/1/16 Faculty Appointment and Promotions Committee, Vanderbilt University Medical Center

### Other Experience and Professional Memberships

1996-present American Academy of Otolaryngology-Head and Neck Surgery
2002-2008 Vanderbilt University Medical Center Institutional Review Board (IRB)

Member 2002-2012; Vice Chair 2003-2004; Chair 2004-2007
2008-present Fellow, Triological Society
2009-present American Otological Society
2009-present American Neurotologyl Society
2009-present Fellow of the American College of Surgeons
2011-present Vanderbilt Initiative in Surgery and Engineering (VISE)

**Honors:**
*Summa Cum Laude*, University of Notre Dame 1988.
National Institute of Health - Medical Scientist Training Fellow 1988-1990, 1992-1996.
American Heart Association Pre-Doctoral Fellow 1990-1991.
First Place Doctoral Student Paper Competition, American Society of Mech Eng Bioeng Division, 1992
Third Place Cardiothoracic Fellow's Research Paper Competition, AHA (West PA Region), 1994.
US Patent #5,537,335, *Fluid Delivery Apparatus and Associated Method*
US Patent #7,794,469, *Adjustable Universal Surgical Platform*
US Patent #7,899,512, *System and Method for Surgical Instrument Disablement via Image-Guided Position Feedback*
US Patent #7,981,122, *Adjustable Surgical Platform and Surgical Instrument Using Same*
US Patent #8,321,636, *Anchor Driver with Assured Seating*
US Patentt #8,380,288, *System and methods of using image-guidance for providing an access to a cochlear of a living subject*
US Patent #8,886,331, *Apparatus and Methods for Percutaneous Cochlear Implantation.*
US Patent pending (claims allowed October 2016) *Methods and Systems for Customizing Cochlear Implant Stimulation and Applications of Same*.
First Place Resident's Research Award, University of North Carolina Womack Surgical Society, 1997.
Second Place Basic Science Research Award, Amer. Acad. of Otolaryngology-Head and Neck Surgery, 1998.
Sam Sanders Award for Basic Science Research, American Academy of Otolaryngic Allergy, 1999.
MED-EL Corporation Clinical Research Award, 2000.
Newton D. Fischer Temporal Bone Dissection Award, 6/2000, 6/2001
American Academy of Otolaryngology-Head and Neck Surgery Honor Award, 10/2009
Grant W. Liddle Award for Outstanding Contributions in Clinical Research, Vanderbilt University Medical Center, 5/2010.
Distinguished Alumni Award, University of Pittsburgh, Department of Bioengineering, March 2012.
Songs for Sound Cochlear Implant Awareness, Success Award, May 2013
Award for Excellence in Resident Education, Vanderbilt University Department of Otolaryngology, June 2013
Web Summit 2015. *Is deafness curable?* Dublin, Ireland. November 4, 2015.
*Magna Lecture: Use of imaging to improve cochlear implantation: from flat plate radiography to image-guided surgery with robots,* Department of Otolaryngology-Head and Neck Surgery, University of San Paulo. December 9, 2015. San Paulo, Brazil.
Creative Minds – US State Department Series. *Wired for Sound: Treating Deafness with Cochlear Implants*. Residence of the United States Ambassador to Ireland. Dublin, Ireland. July 15, 2016 (https://vimeo.com/189220973)
Labadie RF, Fitzapatrick JM. *Image-guided surgery: Fundamentals and Clinical Applications in Otolaryngology.* Plural Publishing, Inc. San Diego, CA. 2016.

### C. Contribution to Science

(1) We have developed a novel way to program cochlear implants using post-operative CT scans to specify the relationship between the neural interface of the cochlear implant electrode array and the endings of the auditory nerve (8$^{th}$ cranial nerve). This work built on prior work (see (a)-(d) below as well as significant publication (5) below) which was discovered during work on significant publication (3). To date, we have applied this technique to over 200 cochlear implant recipients and have long-term data on 101 adult recipients and 11 pediatric recipients. These populations consist of long-term recipients implying that they have achieved maximal benefit from their standard of care cochlear implant mapping. After using the new program for 1 month, 79 of the 101 (79%) and 9 of the 11 pediatric patients (82%) chose to keep the new map either

because of statistically significant improvement in speech understanding or subjective improvement that was deemed significant enough for them to abandon the maps they had been using for, on average, 3 ½ years. This is even more impressive given prior reports that show that cochlear implant recipients are likely to favor existing maps over new experimental maps. We have had cochlear recipients from 25 states travel—at their own expense—to Vanderbilt for such programming. More details of this work can be accessed at http://www.vanderbilt.edu/CAOS/research-projects/slideshow-that-describes-some-recent-research-at-vanderbilt-in-image-guided-cochlear-implant-programming/. For this work, I have served as senior clinical advisor as well as co-inventor of the technology with patents pending.

(a) Reda FA, McRackan TR, Labadie RF, Dawant BM, Noble JH. *Automatic segmentation of intra-cochlear anatomy in post-implantation CT of unilateral cochlear implant recipients*. Med Image Anal 2014 Apr;18(3):605-15. PMID: 24650801.

(b) Noble JH, Labadie RF, Gifford RH, Dawant BM. *Image-guidance enables new methods for customizing cochlear implant simulation strategies*. IEEE Trans Neural Syst Rehabil Eng 2013; 21(5): 820-9. PMID: 23529109.

(c) Noble JH, Labadie RF, Majdani O, Dawant BM. *Automatic Segmentation of Intra-cochlear Anatomy in Convention CT.* IEEE Trans Biomed Eng 2011;58(9):2625-2632. PMID:21708495.

(d) Noble JH, Hedley-William AJ, Sunderhaus L, Dawant BM, Labadie RF, Camarata SM, Gifford RH. *Initial results with image-guided cochlear implant programming in children*. Otol Neurotol 2016 Feb;37(2):e63-9. PMID: 26756157.

(2) When we initially segmented inner ear anatomy as part of significant publication (3), there was a hypothesis in the field that final intracochlear position of cochlear implant electrode arrays had an impact upon audiological performance. Having developed technology that, with few tweaks, could be used to assess this question, we began a clinical study and have established ourselves as leaders in the field developing automatic algorithms to identify most commercially-available cochlear implant electrodes ((a) below) and assessing the relationship between final post-operative position ((b) and (c) below), especially regarding whether electrodes cross the basilar membrane, and audiological performance. This work, for which I have served as senior author and investigator, has resulted in the Harris P. Mosher, MD Award Given in recognition of excellence of a thesis in Clinical Research from the Triological Society for co-author Wanna (c below) for whom I have served as mentor both during his fellowship training as well as his early academic career. Our most recent work reporting on 220 cochlear implant recipients is included as (d).

(a) Zhao Y, Dawant BM, Labadie RF, Noble JH. *Automatic localization of cochlear implant electrodes in CT*. Med Image Comput Comput Assist Interv, 2014;17(Pt 1):331-8. PMID: 25333135.

(b) Schuman TA, Noble JH, Wright CG, Wanna GB, Dawant B, Labadie, RF. *Anatomic Verification of a Novel, Non-rigid Registration Method for Precise Intrascalar Localization of Cochlear Implant Electrodes in Adult Human Temporal Bones Using Clinically-available Computerized Tomography.* Laryngoscope, 2010; 120(11):2277-2283. PMID: 20939074.

(c) Wanna GB, Noble JH, McRackan TR, Dawant BM, Dietrich MS, Watkins LA, Rivas A, Schuman TA, Labadie RF. *Assessment of Electrode Placement and Audiological Outcomes in Bilateral Cochlear Implantation.* Otol Neurotol, 2011 Jan 28. PMID: 21283037.

(d) O'Connell BP, Cakir A, Hunter JB, Francis DO, Noble JH, Labadie RF, Zuniga G, Dawant BM, Rivas A, *Wanna GB. Electrode Location and Angular Insertion Depth Are Predictors of Audiologic Outcomes in Cochlear Implantation*. Otol Neurotol. 2016 Sep;37(8):1016-23. PMID: 27348391

(3) Capitalizing on the underutilization of image-guided surgical technology in otolaryngology, especially at the lateral skull base where anatomy is encased in rigid bone which does not distort during surgical interventions, we began an investigation of the feasibility of replacing a wide-field surgical dissection (mastoidectomy) with a minimally-invasive, image-guide approach in targeting the cochlea for cochlear implantation. This technique progressed from concept ((b) below) to clinical validation ((a) and (c) below) to clinical implementation (significant publication (3)) as well as utility for other applications including implantation of the ossified cochlea ((d) below) and drainage of petrous apex lesioss ((e) below). For this work I have served as PI. A video summarizing our validation studies can be viewed at http://www.vanderbilt.edu/CAOS/videos/. In October of 2016, I received an Investigational Device Exemption from the FDA to continue this investigation.

(a) Labadie RF, Noble JH, Dawant BM, Majdani O, Balachandran R, Fitzpatrick JM. *Clinical validation of percutaneous cochlear implant surgery: initial report.* Laryngoscope 2008;118:1031-39. PMID:18401279.

(b) Labadie RF, Mitchell J, Balachandran R, Fitzpatrick JM. *Customized, Rapid-Production Micro-stereotactic Table for Surgical Targeting: Description of Concept and In-vitro Validation*. Int J Comput Assist Radiol Surg 2009;4(3):273-280. PMID:20033593.
(c) Labadie RF, Balachandran R, Mitchell J, Noble JH, Majdani O, Dawant BM, Bennett M, Haynes DS, Fitzpatrick JM. *Clinical Validation Study of Percutaneous Cochlear Access Using Patient Customized Micro-Stereotactic Frames*. Otol Neurotol 2010;31(1):94-99. PMID:20019561.
(d) Balachandran R, Tsai BS, Ramachandra T, Noble JH, Dawant BM, Labadie RF, Bennett ML. *Minimally-Invasive Image-Guided Access for Drainage of Petrous Apex Lesions*. Otol Neurotol 2014 Apr;35(4):649-55. PMID: 24622019.

(4) Mechatronic surgical interventions involve using automated tools to perform portions of surgical interventions. While in theory this is widely accepted, in practice limited demonstrations have occurred. We undertook the above experiment to show that this concept was empirically reducible (significant work (4)) and further explored in publications (a) – (c) below. Furthermore, we have explored the limits of force needed to cause damage to intracochlear structures (d below) and have shown that this force is approximately at the threshold of human perception (e below) motivating continued development of mechatronic devices.
(a) Kratchman LB, Blachon GS, Withrow TJ, Balachandran R, Labadie RF, Webster RJ. *Design of a Bone-Attached Parallel Robot for Percutaneous Cochlear Implantation*. IEEE Trans Biomed Eng 2011;58(10):2904-10. PMID:21788181.
(b) Dillon NP, Balachandran R, Fitzpatrick JM, Siebold MA, Labadie RF, Wanna GB, Withrow TJ, Webster RJ 3rd. *A Compact, Bone-Attached Robot for Mastoidectomy*. J Med Device. 2015 Sep;9(3):0310031-310037. PMID: 26336572.
(c) Danilchenko A, Balachandran R, Toennies JL, Baron S, Munske B, Fitzpatrick JM, Withrow TJ, Webster RJ, Labadie RF. *Robotic Mastoidectomy*. Otol Neurotol, 2011;32(1):11-16. PMID:21042227.
(d) Schuster D, Kratchman LB, Labadie RF. *Characterization of intracochlear rupture forces in fresh human cadaveric cochleae*. Otol Neurotol. 2015 Apr;36(4):657-6. PMID: 25233332.

(5) Early on in our work with image-guided surgical techniques we recognized the need for automatic segmentation of temporal bone anatomy to improve upon time intensive manual segmentations. Our work built upon prior work at Vanderbilt led by PI Benoit Dawant using statistical atlases to predict location of anatomical structures coupled with image processing of clinical scans containing yet to be identified anatomy. Initially this work involved rigid and non-rigid registration of anatomy encased in bone but subsequently involved more elaborate techniques including development of a novel method to segment tubular structures ((c) below). Statistical shape models were also created to allow advances in the area of significant paper (1). This allowed use of these techniques to assess clinically-relevant anatomy ((a) and (b) below). Most recently, we have shown that rigid + non-rigid registration is significantly better that rigid registration alone when assessing cochlear anatomy. My involvement in the work has been as clinical PI directing the clinical relevance of the work and supervising clinical validation.
(a) Noble JH, Dawant BM, Warren RM, Majdani O, Labadie RF. *Automatic Identification and 3-D Rendering of Temporal Bone Anatomy.* Otol Neurotol 2009;30:436-442. PMID:19339909.
(b) McRackan TR, Reda FA, Rivas A, Noble JH, Dietrich MS, Dawant BM, Labadie RF. *Comparison of cochlear implant relevant anatomy in children versus adults.* Otol Neurotol. 2012 Apr;33(3):328-34. PMID:22377644.
(c) Noble JH, Warren FM, Labadie RF, Dawant BM. *Automatic segmentation of the facial nerve and chorda tympani in CT images using spatially dependent feature values.* Medical Physics 2008;35(12): 5375-84. PMID:19175097.
(d) Cakir A, Labadie RF, Zuniga MG, Dawant BM, Noble JH. *Evaluation of Rigid Cochlear Models for Measuring Cochlear Implant Electrode Position*. Otol Neurotol. 2016 Dec;37(10):1560-1564. PMID: 27755453.

**Complete List of Published Work in MyBibliography:**
https://www.ncbi.nlm.nih.gov/sites/myncbi/1Pksp2DTx5vkN/bibliography/47354331/public/?sort=date&direction=descending

**D. Research Support**
*Ongoing Research Support:*
NIDCD 2R01DC008408-11 7/1/12 – 3/31/23

Clinical Validation and Testing of Percutaneous Cochlear Implantation
The major goal of this study is to validate a new technique for cochlear implantation. This technique utilizes image–guided surgery to reduce a wide–field, time intensive procedure to a minimally–invasive procedure.

NIDCD 1R01DC012593-01A1 (PI: Webster, co-I: Labadie) 12/1/17 – 11/30/19
Non-Invasive Transnasal Diagnosis of Inner Ear Disease
The goal of this project is to provide guidance during the device design phase of the proposed work (Aim 1).

NIDCD 1 R01 DC014037-01 (PI: Noble, co-I: Labadie) 6/1/2014 – 5/31/2019
Image-Guided Cochlear Implant Programming Techniques
The goal of this project is to develop and evaluate new image-guided cochlear implant programming strategies that use objective information acquired from clinical images to determine patient customized frequency, current steering, and current focusing settings that lead to better hearing outcomes.

NIDCD 1 R01 DC014462-01A1 (PI: Dawant, Co-I: Labadie) 11/01/15-10/31/20
Computer-Assisted, Image-Guided Programming of Cochlear Implant Evaluation
The goals of this project are to develop on-line deployable tools to efficiently implement Image-Guided Cochlear Implant Programming (IGCIP) both within and outside of our home institution on a large scale. Additionally, we will construct and analyze the resultant large data base to identify factors that affect performance with IGCIP to facilitate further improvement in its efficacy.

*Completed research support*:

None

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Jack H. Noble

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Assistant Professor of Electrical Engineering and Computer Science

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Vanderbilt University | B.E.<br>M.S.<br>Ph.D. | 05/2007<br>12/2008<br>05/2011 | Electrical Engineering |

### A. Personal Statement

In ongoing collaborative studies with Vanderbilt colleagues for which I am the principal investigator, I have developed algorithms and software systems that permit determining the position of small scale intra-cochlear anatomy and the precise intra-cochlear locations of cochlear implant (CI) electrodes in patient CT scans. We have demonstrated our methods to have a high degree of accuracy. We have used them to show that sub-optimal intra-cochlear positioning of the electrodes is associated with poorer outcomes, and we have shown these techniques can be used to implement Image-Guided Cochlear Implant Programming (IGCIP) techniques, where CI processor settings are determined based on intra-cochlear electrode position to improve hearing outcomes. The main goal of the current project is to evaluate the effects of IGCIP techniques on basic auditory function, speech understanding, language abilities, speech production, and literacy outcomes in pediatric CI recipients. This project is of significant clinical interest as natural hearing quality and fidelity are rare among pediatric CI recipients, and any strategies that improve outcomes can have high impact on sound-quality-of-life. I have over 10 years of experience in the area of medical image processing and analysis. I will be site PI at Vanderbilt University and will oversee development, maintenance, and analysis of the imaging data repository and for the creation of IGCIP plans for the 60 cochlear implant recipients that will participate in this study. I will supervise with Dr. Dawant a staff engineer who will maintain the database, assist in the creation of plans, and perform any modification of the planning software necessary to support this project. As the primary investigator responsible for developing the image analysis tools that will be used, and as a successful PI on other previous and ongoing projects, I have the expertise necessary to fulfill my responsibilities for this project.

### B. Positions and Honors

**Positions and Employment**

2018-Present Assistant Professor of Electrical Engineering & Computer Science, Vanderbilt University
2015-Present Research Assistant Professor of Hearing & Speech Sciences, Vanderbilt University
2014-Present Research Assistant Professor of Otolaryngology – Head & Neck Surgery, Vanderbilt University
2011-2017 Research Assistant Professor of Electrical Engineering, Vanderbilt University

**Honors**

2017 Guest Associate Editor for SPIE Journal of Medical Imaging Special Issue on Image-Guided Procedures, Robotic Interventions, and Modeling
2016 Communication Services Award from the Dept. of Hearing and Speech Sciences at the Vanderbilt Bill Wilkerson Center
2015-2017 Awarded NIH Clinical Research Loan Repayment Program Grant (L30)
2014 US Patent pending, *An artifact-robust, shape library-based algorithm for automatic segmentation of inner ear anatomy in post-cochlear-implantation CT*

2013 US Patent pending, *Method for Automatic Segmentation of Intra-Cochlear Anatomy in Post-Unilateral-Implantation CT*
2013 Awarded $1000 first prize for best poster at the Vanderbilt Bill Wilkerson Center for Otolaryngology and Communication Sciences Combined Poster Session
2012-2014 Awarded NIH Clinical Research Loan Repayment Program Grant, L30DC012689
2012 US Patent pending #61/619,824, *System and methods of cochlear implant mapping based on intracochlear position of electrode arrays and applications of same*
2011 US Patent #8,073,216, *System and methods for automatic segmentation of one or more critical structures of the ear*
2010 Top ten finalist in the best student paper competition at the SPIE Conference on Medical Imaging
2008-2011 NIH/NIDCD Pre-doctoral Fellowship
2007-2011 Awarded IBM Engineering Graduate Scholarship
2007 *Magna Cum Laude* with Honors, Vanderbilt University
2006 Awarded stipend from the Vanderbilt Undergraduate Summer Research Program to conduct the research project "Automatic identification of the facial nerve in CT for percutaneous cochlear implant surgery"

**Student Honors (Mentor)**

2017 Runner up in the best student paper competition (from over 50 submissions) at the SPIE Conference on Medical Imaging 2017 (Ahmet Cakir)
2014-2015 Awarded Vanderbilt Initiative in Surgery and Engineering (ViSE) Fellowship (Yiyuan Zhao)
2013 Awarded Vanderbilt University School of Engineering Summer Undergraduate Research Program Fellowship (Rebecca Turok)
2012 Top ten finalist in the best student paper competition at the SPIE Conference on Medical Imaging 2012 (Fitsum Reda)

**Grant Reviewing**

2018 Served on the NIH/NIDCD Translational R01 review [redacted] study section.
2017 Served on the NIH/NIDCD Hearing and Balance Fellowships Review [redacted] study section.
2016 Served on the NIH/NIDCD Translational R01 review [redacted] study section.
2016 Served as reviewer for Action on Hearing Loss research grant program.

**Journal Editorial Board Service and Reviewing**

Associate Editor: 2018 SPIE Jour. of Med. Imag. Spec. Iss. on Image-Guided Proc., Robotic Interv., and Modeling
Journal of Medical Imaging
International Journal of Computer Aided Radiology and Surgery
Medical Image Analysis
International Journal of Medical Robotics and Computer Assisted Surgery
I.E.E.E. Transactions on Biomedical Engineering
Physics in Medicine and Biology
Medical Physics
Medical Engineering & Physics
Otology & Neurotology
Audiology & Neurotology
European Archives of Oto-Rhino-Laryngology

**Other Experience and Professional Memberships**

2008- Member, International Society for Optics and Photonics (SPIE)
2008- Member, Institute of Electrical and Electronic Engineers (IEEE)
2008- Member, Medical Image Computing and Computer Assisted Intervention Society (MICCAI)

## C. Contribution to Science

1. In my earlier work I developed algorithms and techniques that can automatically and accurately identify many of the important anatomical structures of the ear in CT scans. Prior to these publications, no methods for automatically localizing ear anatomy had been developed and few studies existed that quantified 3D ear

anatomy due to the difficulty in manual image analysis. The published methods have been transformative in the Otology community as they in many ways have lowered the barrier for use of patient-specific image information in Otology applications. These techniques have enabled for the first time large scale analysis of anatomical shape variations, development of computer assisted surgery planning methods, and development of post-operative assessment systems. I served as the primary or senior investigator in all these studies.

a. Noble, J.H., Labadie, R.F., Majdani, O., Dawant, B.M., “Automatic segmentation of intra-cochlear anatomy in conventional CT”, *IEEE Trans. on Biomedical. Eng*., Vol. 58, No. 9, pp. 2625-32, 2011. PMC3804019
b. Noble, J.H., Warren, F.M., Labadie, R.F., Dawant, B.M., "Automatic segmentation of the facial nerve and chorda tympani in CT images using spatially dependent feature values," *Med. Phys*., 35:5375-5384, 2008. PMC2673604
c. Noble, J.H., Dawant, B.M., Warren, F.M., Labadie, R.F., "Automatic Identification and 3D Rendering of Temporal Bone Anatomy," *Otol & Neurotol*., 30(4):436-42, 2009. PMC4437534
d. Reda, F.A., McRackan T.R., Labadie, R.F., Dawant, B.M., Noble JH, “Automatic segmentation of intra-cochlear anatomy in post-implantation CT of unilateral cochlear implant recipients,” *Medical Image Analysis*, vol. 18(3), pp. 605-15, 2014. PMC4410997

2. Other early and ongoing work has aimed at developing image processing fundamentals that permit localizing tubular structures in medical images. Tubular structures, such as nerves and vessels, are found throughout the body and their localization is crucial for a variety of application specific analyses. My work in this area has led to several novel algorithms that permit localization of a variety of structures. I served as the primary or co-investigator in these studies.

a. Noble, J.H., Dawant, B.M., “An atlas-navigated optimal medial axis and deformable model algorithm (NOMAD) for the segmentation of the optic nerves and chiasm in MR and CT images,” *Medical Image Analysis*, Vol. 15, No. 6, pp. 877-884, 2011. PMC3191306
b. Noble, J.H. and Dawant, B.M., 2011, “A New Approach for Tubular Structure Modeling and Segmentation Using Graph-Based Techniques,” *Lecture Notes in Computer Science – Proceedings of MICCAI*, 6893, pp. 297-304. PMC4184473
c. Ding, S., Miga, M.I., Noble, J.H., Cao, A., Dumpuri, P., Thompson, R.C., Dawant, B.M., "Semi-automatic registration of pre- and post- brain tumor resection laser range data: method and validation," *IEEE Trans Biomed Eng*., 56(3):770-80, 2008. PMC2791533
d. Reda, F.A., Noble, J.H., Rivas, A., McRackan, T.R., Labadie, R.F., Dawant, B.M., “Automatic segmentation of the facial nerve and chorda tympani in pediatric CT scans,” *Medical Physics* 38, pp. 5590-5600, 2011. PMC3208411

3. Our group has worked to develop novel systems for stereotactic framed-guided cochlear implantation procedures and deep brain stimulator placement procedures. Stereotactic frame guided surgery offers significant benefits over standard of care in terms of precision and invasiveness. I developed automated surgical path planning techniques that find probabilistically safe and effective surgical paths. These techniques were the first of their kind in that they permit estimating the probability of success or failure. These publications report the novel path planning methods and how they are used in these image-guided surgery systems. I was primary or co-investigator in these studies.

a. Noble, J.H., Majdani, O., Labadie, R.F., Dawant, B.M., Fitzpatrick, J.M., "Automatic Determination of Optimal Linear Drilling Trajectories for Cochlear Access Accounting for Drill-Positioning Error," *Intl. J. of Med. Robotics and Comp. Assist. Surg*., 6(3):281-290, 2010. PMC2933923
b. Liu, Y., Konrad, P., Neimat, J., Tatter, S., Yu, H., Datteri, R., Landman, B., Noble, J.H., Pallavaram, S., Dawant, B.M., and D’Haese, P., “Multi-Surgeon, Multi-Site Validation of a Trajectory Planning Algorithm for Deep Brain Stimulation Procedures,” *IEEE Trans. on Biomedical Engineering*, vol. 61(9), pp. 2479-87, 2014. PMC4142093
c. Labadie, R.F., Noble, J.H., Dawant, B.M., Balachandran, R., Majdani, O., Fitzpatrick, J.M., “Clinical validation of percutaneous cochlear implant surgery: initial report,” *Laryngoscope*, 118:1031-9, 2008. PMC4453765

d. Labadie, R.F., Balachandran, R., Mitchell, J., Noble, J.H., Majdani, O., Haynes, D.S., Bennett, M., Dawant, B.M., Fitzpatrick, J.M., "Clinical Validation Study of Percutaneous Cochlear Access Using Patient Customized Micro-Stereotactic Frames," *Otology & Neurotology*, 31(1):94-99, 2010. PMC2845321

4. Cochlear implants are neural prosthetic devices used to treat profound hearing loss. Outcomes with cochlear implants are highly variable. Placement of the device is one factor linked to outcomes but has not been well understood. I developed automated image processing techniques to analyze placement of the electrodes, permitting large scale investigation of how hearing outcomes relate not only to device placement, but also to device design and programming. The following publications detail the methodology and how it was validated as well as some of the large scale investigations we have performed. I was senior, principal, or co-investigator in these studies.

    a. Zhao, Y., Dawant, B.M., Labadie, R.F., and Noble, J.H., "Automatic Localization of Cochlear Implant Electrodes in CT," *Lecture Notes in Computer Science – Proceedings of MICCAI*, vol. 8673, pp. 331-8, 2014. PMC4426961
    b. Cakir A., Labadie R.F., Dawant B.M., Noble J.H., "Evaluation of cochlear anatomy models for determining intra-cochlear electrode position," Otology & Neurotology, 37(10):1560-1564. 2016. PMC5240585
    c. Noble, J.H. and Dawant, B.M., "Automatic graph-based localization of cochlear implant electrodes in CT," Lecture Notes in Computer Science – Proceedings of MICCAI, vol. 9350, pp. 152-9, 2015. PMC4854292
    d. Wanna, G.B., Noble J.H., Carlson, M.L., Gifford, R.H., Dietrich, M.S., Haynes, D.S. Dawant, B.M., and Labadie, R.F., "Impact of Electrode Design and Surgical Approach on Scalar Location and Cochlear Implant Outcomes," *Laryngoscope*, vol. 124(S6), pp. S1-7, 2014. PMC4209201

5. Much of my recent work has focused on developing techniques for image-guided cochlear implant programming (IGCIP), where information from patients' CT images is used to customize the settings that control how the implant operates. Leveraging much of the ear anatomy and cochlear implant image analysis techniques developed above, I was able to propose, develop, and clinically test the first method for IGCIP. IGCIP is exciting because the reward is high--our studies have shown IGCIP significantly improves hearing outcomes for cochlear implant recipients--while risks are low—IGCIP requires only making a simple and reversible change of settings without any additional surgical procedures. The following publications report the development of IGCIP and the results of recent clinical tests. This is an emerging research area, and we are in progress with publications reporting new clinical studies and IGCIP strategies. I was the principal investigator in these studies.

    a. Noble, J.H., Gifford, R.H., Labadie, R.F., Dawant, B.M., 2012, "Statistical Shape Model Segmentation and Frequency Mapping of Cochlear Implant Stimulation Targets in CT," N. Ayache et al. (Eds.): MICCAI 2012, Part II, LNCS 7511, pp. 421-428. 2012. PMC3559125
    b. Noble JH, Labadie RF, Gifford RH, Dawant BM, "Image-guidance enables new methods for customizing cochlear implant stimulation strategies," *IEEE Trans Neural Syst Rehabil Eng.* vol. 21(5):820-9, 2013. PMC3769452
    c. Noble JH, Gifford RH, Hedley-Williams AJ, Dawant BM, and , Labadie RF, "Clinical evaluation of an image-guided cochlear implant programming strategy," *Audiology & Neurotology*, vol. 19, pp. 400-11, 2014. PMC4305276
    d. Noble JH, Hedley-Williams AJ, Sunderhaus LW, Dawant BM, Labadie RF, Gifford RH, "Initial results with image-guided cochlear implant programming in children," *Otology & Neurotology* 37(2), pp. 69-9, 2016. PMC4849538

**Complete List of Published Work in MyBibliography (Over 50 peer-reviewed publications):**
http://www.ncbi.nlm.nih.gov/sites/myncbi/jack.noble.1/bibliography/41146802/public/?sort=date&direction=ascending

## D. Research Support

### Ongoing Research Support

5R01DC014037 (Noble) 6/01/14-05/31/19
NIH/NIDCD
Image-guided cochlear implant programming techniques
The goals of this project are to develop and evaluate new patient-customized, Image-Guided Cochlear Implant Programming (IGCIP) strategies that could provide objective information to the programming process and lead to programs that better approximate natural hearing performance.
Role: Principal Investigator

5R01DC014462 (Dawant) 12/01/15-11/30/20
NIH/NIDCD
Computer-assisted, image-guided programming of Cochlear Implants
To mature the system we have developed for patient-customized, image-guided cochlear implant programming to produce a system that will be clinically deployable, thus increasing the number of cochlear implant recipients who can benefit from this technology.
Role: Co-investigator, responsible for overseeing and conducting some software development tasks

1R01 DC15798 (Noble) 09/01/16-08/31/19
NIH/NIDCD (Subcontract from U of MD)
*Single-Sided Deafness Cochlear Implants for Functioning in Complex Auditory Environments*
The subcontract of this award is to Jack Noble (co-I, Vanderbilt) is the world's leading expert in reading x-rays (CT scans) to determine cochlear implant location in the head, a critical piece to this work.

1R21DC16153 (Webster) 09/01/17-08/31/19
NIH/NIDCD
*Transnasal Diagnosis of Middle Ear Disease*
The objective of this proposal is to replace exploratory surgery with a novel natural-orifice approach to diagnose and surveil middle ear disease.

### Previous Research Support

5R01 DC008408 (Labadie) 07/13/12-06/30/17
NIH/NIDCD
Clinical Validation and Testing of Percutaneous Cochlear Implantation
This application is to propose a multi-center study looking at the use of patient-specific drill guides built via rapid-prototyping based on pre-operative CT scans.
Role: Co-Investigator, responsible for some of the segmentation and planning software tasks of the project

1R21 EY024036 Landman (PI) 12/01/13-11/30/16
NIH/NEI
Quantitative Image Analysis Techniques for Optic Nerve Disease
To translate medical imaging computing procedures from the neuroimaging community to provide robust, quantitative tools for assessing the optic nerve (ON) on clinical and research imaging sequences.
Role: Co-Investigator, responsible for overseeing some segmentation development tasks

5R21 DC012620 Noble (PI) 07/01/12-06/30/15
NIH/NIDCD
Image-based Frequency Reallocation for Optimizing Cochlear Implant Programming
To develop and assess the clinical utility of an approach for determining the position of implanted cochlear implant electrodes relative to the nerves of the Spiral Ganglion for CI tuning assistance.
Role: Principal Investigator

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Benoit Dawant

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Cornelius Vanderbilt Professor of Engineering, Professor of Electrical Engineering, Professor of Biomedical Engineering, Professor of Radiology and Radiological Sciences, Vanderbilt University

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Catholic University of Louvain, Belgium | MSEE | 1982 | Electrical Engineering |
| University of Houston, TX | Ph.D. | 1987 | Systems Engineering |

### A. PERSONAL STATEMENT

I am the founding director of the Vanderbilt Initiative in Surgery and Engineering that is an interdisciplinary, trans-institutional center whose mission is the creation, development, implementation, clinical evaluation and commercialization of methods, devices, algorithms, and systems designed to facilitate interventional processes and their outcome. I am also the director of the Medical Image Processing laboratory at Vanderbilt where the image processing algorithms supporting the IGIP technique have been developed. I have more than 20 years of experience in the area of medical image processing and analysis. I have also more than 10 years of experience with large data repositories and associated processing pipelines, and with the clinical deployment of software designed for assisting surgical and post-surgical processes. I will supervise the software engineer/database specialist who has developed the current IGCIP database and associated web-based portals that permit uploading images, storing plans, setting calendars, and communication between study personnel. She will be responsible for maintaining the database and for the transfer of images and plans. She will also assist in the creation of plans and on the modification of the planning tools and the database necessary to support new IGCIP techniques.

### B. POSITIONS AND HONORS

**Positions and Employment**

1988-1994 Assistant Professor of Electrical Engineering, Vanderbilt University
1994-2002 Associate Professor of Electrical and Computer Engineering, Vanderbilt University 2002-Present Professor of Electrical and Computer Engineering
2002-Present Professor of Radiology and Radiological Sciences
2009-Present Professor of Biomedical Engineering
2011-Present Cornelius Vanderbilt Professor of Engineering
2011-Present Director, Vanderbilt Initiative in Surgery and Engineering

Honors

1994: Recipient of the Japanese Government Research Award for foreign specialist in the area of medical imaging.
1996-2004: Associate Editor, IEEE Transactions on Biomedical Engineering
1996 (Fall): Senior visiting fellow, Katholieke Universiteit Leuven, Depts. of Electrical Engineering and Radiology, Leuven, Belgium
1999: Co-Guest Editor, Special Section on Data Fusion, IEEE Transactions on Biomedical Engineering
1999: Invited Guest Editor, IEEE Transactions on Information Technology in Biomedicine

2000: Recipient of the most often cited paper award, IEEE Transactions on Medical Imaging (award received for paper published in 1993)
2001-2008: Member of the steering Committee, IEEE Transactions on Medical Imaging, Chair of this committee from 2005-2008
2002 (Summer) Visiting Professor, Université Catholique de Louvain (UCL) 2010 Fellow, *IEEE*

## C. CONTRIBUTION TO SCIENCE

For the last twenty years, I have worked in the area of medical image processing and analysis. I have worked at the interface between engineering and medicine. My laboratory has developed both basic image processing algorithms and systems that have been clinically translated, integrated into the clinical flow, and commercialized.

**Segmentation:** Early in my career I worked on the problem of tissue classification in MR images of the head. While working on this problem I identified image intensity inhomogeneity in MR images as an important problem to be addressed. Together with graduate student [redacted] I developed a method for the correction of this artifact, which was reported in the IEEE Transactions on Medical Imaging (TMI) paper entitled "Correction of intensity variations in MR images for computer-aided tissue classification" [Daw93]. This paper has drawn interest from the community and I later received an IEEE TMI award for authorship of the journal's most frequently cited paper published in 1993. This award recognizes this paper as "a classic paper in the field of medical imaging, with exceptional originality and enduring impact". Using this technique to correct for intensity inhomogeneity, an automatic MR method for the segmentation of multi-modal MR images into white matter, gray matter, cerebrospinal fluid, and white matter lesions (these are abnormalities thought to be correlated with Alzheimer's disease) was developed and reported in the IEEE TMI paper entitled "Morphometric analysis of white matter lesions in MR images: method and validation" [Zij94]. This paper was published in 1994 and is still being cited (505 Web of Science citations in total and 42 in 2013). My laboratory has also developed methods for the automatic segmentation of the liver [Her05] that have been patented (US patent 7,519,209 "System and methods of organ segmentation and applications of same") and included in a commercial system for image-guided liver surgery developed by a spinoff called Pathfinder, Inc. that has now been acquired by Analogic Corporation as well as techniques for the segmentation of radiation sensitive structures in the head and neck for radiotherapy planning [Dee11].


- [Daw93] Dawant BM, Zijdenbos, AP., and Margolin R, "Correction of Intensity Variations in MR Images for Automatic Tissue Characterization", IEEE Transactions on Medical Imaging. 12(4), 1993, pp. 770-781; PMID: 18218473, No PMC, published prior to 2007
- [Zij94] Zijdenbos AP., Dawant BM., and Margolin R. "Morphometric Analysis of White Matter Lesions in MR Images: Method and Validation" IEEE Transactions on Medical Imaging, 13(4), pp.716-724, 1994; PMID: 18218550, No PMC, published prior to 2007.
- [Her05] Hermoye L., Laamari I., Cao Z., Annet L., Lerut J., Dawant BM., and Van Beers BE., "Semi-automatic liver volumetry: validation in living donors for liver transplantatikon", Radiology 234 (1), pp. 171-178, 2005, PMID: 15564393, No PMC, published prior to 2007
- [Dee11] Deeley, MA, Chen A, Datteri R, Noble JH, Cmelak AJ, Donnelly EF, Malcolm AW, Moretti L, Jaboin J, Niermann JK, Yang ES, Yu DS, Yei F, Koyama T , Ding GX, Dawant BM. "Comparison of Manual and Automatic Segmentation Methods for Brain Structures in the Presence of Space-Occupying Lesions: A Multi-Expert Study." Phys Med Biol 56, no. 14 (Jul 21 2011): 4557-77, PMC3153124

**Registration:** Although early in my career, I focused on segmentation, my research interest subsequently evolved to include image registration as I identified this as a way to incorporate a-priori information into the segmentation process. I initiated a collaboration with [redacted] who had proposed a method for the non-rigid registration of images. I demonstrated that automatic segmentation of internal brain structures using a combination of rigid and non-rigid registration techniques was indeed achievable. This was reported in the TMI paper entitled “Automatic 3-D segmentation of internal structures of the head in MR images using a combination of similarity and free-form transformations: Part I, methodology and validation on normal subjects” [Daw99].This paper also had a lasting effect on the field and is still being cited. Although results obtained in this study were satisfactory, the approach suffers from one major drawback: it is only applicable to images with comparable intensity characteristics. With mathematician colleague [redacted] and graduate student [redacted] I began working on the development of a multi-modal non-rigid registration method. This led to a novel spline-based method for non-rigid registration reported in the paper entitled “The adaptive bases algorithm for intensity-based nonrigid image registration” [Roh03]. This approach is different from the ones that had been proposed in the literature at that point in one key aspect. The algorithm operates on an irregular grid. It permits the spatial adaptation of the compliance of the transformation and local optimization, which has been shown to improve convergence properties and execution speed. This paper has been published in 2004, it has been cited 226 times with 19 citations in 2014. Registration techniques my laboratory developed have been used to integrate 3D mass spectrometry images and in vivo magnetic resonance imaging [Sin08] as well as for longitudinal studies of breast images [Li09].


- [Daw99] Dawant BM., Hartmann SL, Thirion J-P., Maes F., Vandermeulen D., and Demaerel P. “Automatic 3D segmentation of internal structures of the head in MR images using a combination of similarity and free form transformations: Part I, methods and validation on normal subjects”, IEEE Transactions on Medical Imaging , 18(10), 897-908, 1999, No PMC, published prior to 2007
- [Roh03] Rohde G.K., Aldroubi A., Dawant B.M., “The adaptive bases algorithm for intensity-based nonrigid image registration.” IEEE Trans Med Imaging, 2003 Nov; 22(11): 1470-9; No PMC, published prior to 2007
- [Sin08] Sinha TK., Khatib-Shahidi S., Yankeelov TE., Mapara K., Ehtesham M., Cornett DS., Dawant BM., Caprioli RM., Gore J.C., “Integrating spatially resolved three-dimensional MALDI IMS with in vivo magnetic resonance imaging”, Nature Methods, 5(1), pp. 57-59, 2008; PMC2649801
- [Li09] Li X, Dawant BM, Welch EB, Chakravarthy AB, Freehardt D, Mayer I, Kelley M, Meszoely I, Gore JC, Yankeelov TE. “A Nonrigid Registration Algorithm for Longitudinal Breast MR Images and the Analysis of Breast Tumor Response”. Magn Reson Imaging. 2009 Nov;27(9):1258-70; PMC2763059


**Assistance for the planning, placement, and programming of Deep Brain Stimulators (DBS)**. Over the last ten years my laboratory has developed a system designed to assist clinical teams that perform DBS procedures that are used to treat movement disorders such as Parkinson’s disease. In the paper entitled “Computer-aided Placement of deep brain stimulators: From planning to intra-operative guidance” published in 2005 [Dha05] we demonstrated that automated selection of the implantation target was feasible and at least as good as a trained neurosurgeon. We also obtained a patent for this work (US patent 7,167,760, “Apparatus and methods for optimal placement of deep brain stimulator”). More recently we showed that automating the complete trajectory, i.e., both the entry and target points, planning was also achievable [Liu14] and that computer-assistance is of value for programming the implant [Phi14]. Supported by three NIH R01s we developed a complete system to assist in all phases of the procedure, which is now integrated into the clinical flow at Vanderbilt. This system has been described in the paper entitled “Cranial Vault and its Crave tools: A clinical computer assistance system for deep brain stimulation (DBS) therapy” [Dha12]. In parallel, together with my colleagues [redacted], I create a spinoff company to commercialize and distribute the research system developed at Vanderbilt. Supported by one NIH STTR Phase I and one STTR Phase II, this small concern obtained FDA clearance for the pre-operative and intra-operative components of the system, which are currently distributed by FHC, Inc. under the name WayPoint Navigator (http://www.fh-co.com/products/clinical-systems/waypoint-navigator ). It also obtained CE clearance for the post-operative component that is currently distributed by Medtronic, Inc. We are currently collaborating with the major DBS centers in the US to field our research system at these sites and to create what we envision will become a central resource for DBS procedures.

- [Dha05] D'Haese P-F., Cetinkaya E., Konrad PE., Kao Ch., and Dawant BM., "Computer-aided placement of deep brain stimulators: from planning to intra-operative guidance", IEEE Transactions on Medical Imaging, 24(11), pp. 1469-1478, 2005; No PMCID; published before 2007
- [Liu14] Liu Y, Konrad PE, Neimat JS, Tatter SB, Yu H, Datteri RD, Landman BA, Noble JH, Pallavaram S, Dawant BM, DHaese PF. "Multisurgeon, multisite validation of a trajectory planning algorithm for deep brain stimulation procedures". IEEE Trans Biomed Eng. 2014 Sep;61(9):2479-87; PMC4142093
- [Dha12] D'Haese PF, Pallavaram S, Li R, Remple MS, Kao C, Neimat JS, Konrad PE, Dawant BM. "Cranialvault and Its Crave Tools: A Clinical Computer Assistance System for Deep Brain Stimulation (DBS) Therapy". Med Image Anal. 2012 Apr;16(3):744-53; PMC3021628
- [Phi14] Phibbs FT, Pallavaram S, Tolleson C, D'Haese PF, and Dawant BM, "Use of efficacy probability maps for the post-operative programming of deep brain stimulation in essential tremor", Parkisonism and Related disorders, 2014, 20(12), 1341-1344; PMC4039015


**Image-guided programming of cochlear implants.** Cochlear implants are used to treat patients who suffer from profound hearing loss. Current technology yields very good results for the vast majority but a significant number of users receive marginal benefit, and even the best performers complain that the fidelity of natural hearing is not reproduced. One of the issues is the difficulty to come up with optimal parameter settings. In current clinical practice, this is done based on subjective feedback provided by the patient to the audiologist. Together with former graduate student and now colleague Dr. Noble and clinical colleague Dr. Labadie I have developed a series of unique image processing algorithms that permit the automatic segmentation off all internal structures in the inner ear as well the localization of the electrode [Nob08, Nob09]. Thanks to these algorithms, which have been patented (US patent 8,073,216, "System and methods for automatic segmentation of one or more critical structures of the ear"), programming of the electrodes can now be accomplished based on objective information, e.g., relative position of each contact and the nerves they stimulate. We have developed a new programming strategy that makes use of this information, which has been described in the paper entitled "Image-guidance enables new methods for customizing cochlear implant stimulation strategies" [Nob13]. We have conducted a large scale evaluation study of this strategy. Long-term recipients (some have been implanted several years ago) who had been programmed using the current clinical protocol and for whom programming parameter settings were considered to be optimal were enrolled. These recipients were re-programmed using the image-guided protocol we have developed and outcomes prior to and after re-programming were compared. In the paper entitled "Clinical evaluation of an image-guided cochlear implant programming strategy" [Nob14] we report results that show in 68 adult CI recipients that our image-guided approach yields significant improvement in speech understanding in both quiet and noise as well as improved spectral resolution. These results indicate that image guidance can improve hearing outcomes for many existing CI recipients without requiring additional surgery or the use of 'experimental' stimulation strategies, hardware or software. At the time of writing, we have used IGCIP to re-program well over 200 adult ears. We have seen 178 adult study participants (197 ears) for both the baseline and post-IGCIP visits and 135 or 68.5% of the re-programmed patients chose to keep the IGCIP settings.


- [Nob08] Noble JH, Warren FM, Labadie RF, Dawant BM. "Automatic Segmentation of the Facial Nerve and Chorda Tympani in Ct Images Using Spatially Dependent Feature Values". Med Phys. 2008 Dec;35(12):5375-84, PMC2673604
- [Nob09] Noble JH, Dawant BM, Warren FM, Labadie RF. Automatic Identification and 3D Rendering of Temporal Bone Anatomy. Otol Neurotol. 2009 Jun;30(4):436-42; NIHMSID 685248, PMCID in process
- [Nob13]Noble JH, Labadie RF, Gifford RH, and Dawant BM, "Image-Guidance Enables New Methods for Customizing Cochlear Implant Stimulation Strategies" IEEE Transactions on Neural Systems and Rehabilitation Engineering, 2013, 21(5), pp. 820-829, PMC3769452
- [Nob14] Noble JH, Gifford RH, Hedley-Williams AJ; Dawant BM, and Labadie RF, "Clinical Evaluation of an Image-Guided Cochlear Implant Programming Strategy", Audiology and Neuro-Otology, 2014, 19(6), pp. 400-411, PMC4305276


**LINK TO BIBLIOGRAPHY**

http://www.ncbi.nlm.nih.gov/sites/myncbi/benoit.dawant.1/bibliography/40737322/public/?sort=date&direction=ascending

## D. RESEARCH SUPPORT

### Ongoing Research Support

5R01NS095291-10 (Dawant/D'Haese) 09/30/15-07/31/19
NINDS
Computer-Assisted Functional Neurosurgery
The goal of this project is to continue the clinical evaluation of our system, expand its functionality, and deploy it at collaborating sites. Our long term goals are to develop and field (1) the first integrated DBS solution that will permit seamless exchange of information between all phases of the procedure and (2) a shared and global resource that will allow rapid dissemination of discovery and outcomes related to specific brain targets. It will thus be a catalyst that can both speed up discoveries in neurological sciences and improve clinical processes

5R01DC014462-02 (Dawant) 12/01/15-11/30/20
NIDCD
Computer-assisted, image-guided programming of Cochlear Implants
The goals of this project are to develop an Image-Guided Cochlear Implant Programming (IGCIP) strategy that can substantially and sometime dramatically improve hearing in long term CI users without requiring an additional surgical procedure and to conduct a large scale clinical validation both at Vanderbilt and at collaborating sites to discover factors that affect the performance of the method and further improve it.

5R01DC014037-03 (Noble) 06/01/14-05/31/19
NIH/NIDCD
Image-guided cochlear implant programming techniques
The goal of this project is to develop and evaluate new image-guided cochlear implant programming strategies that use objective information acquired from clinical images to determine patient customized frequency, current steering, and current focusing settings that lead to better hearing outcomes.

### COMPLETED

5R01NS049251-10 (Miga) 08/01/04-4/30/16
NINDS
Multimodal Registration of the Brain's Cortical Surface.3
Development of methods and techniques to compensate for brain shift during tumor resection surgery.

# BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Dietrich, Mary S.

eRA COMMONS USER NAME (agency login): [redacted]

POSITION TITLE: Professor, Statistics & Measurement

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

| INSTITUTION AND LOCATION | DEGREE (if applicable) | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Bethel College, North Newton, Kansas | BS | 05/1979 | Psychology |
| Fort Hays State University, Hays, Kansas | MS | 12/1986 | Experimental Psychology |
| Vanderbilt University, Nashville, Tennessee | PHD | 05/1996 | Statistics/Measurement |

## A. PERSONAL STATEMENT

As a Professor in the School of Medicine (Department of Biostatistics, Vanderbilt Ingram Cancer Center, Department of Psychiatry) and in the School of Nursing at Vanderbilt University, I have broad-ranging and extensive experience in biostatistical collaborations and applications including collaborations with Dr.Gifford and other researchers developing and evaluating image-guided cochlear implant programming (IGCIP) as noted below.

Gifford RH, Loiselle L, Natale S, Sheffield SW, Sunderhaus LW, **Dietrich MS**, Dorman MF. Speech understanding in noise for adults with cochlear implants: effects of hearing configuration, source location uncertainty, and head movement. *Journal of Speech Language and Hearing Research*. [In press].

Gifford RH, Noble JH, Camarata SM, Sunderhaus LW, Dwyer RT, Dawant BM, **Dietrich MS**, Labadie RF. (in press). The relationship between spectral modulation detection and speech recognition: adult versus pediatric cochlear implant recipients. *Trends in Hearing.* [In press].

McRackan TR, Noble JH, Wilkinson EP, Mills D, **Dietrich MS**, Dawant BM, **Gifford RH,** Labadie RF. Implementation of image-guided cochlear implant programming at a distant site. *Otolaryngology – Head and Neck Surgery*; 2017 May; 156(5); 933-937. PMID: 28374640.

Wanna GB, Noble JH, **Gifford RH, Dietrich MS**, Sweeney AD, Zhang D, Dawant BM, Rivas A, Labadie RF. Impact of intrascalar electrode location, electrode type, and angular insertion depth on residual hearing in cochlear implant patients: Preliminary results. *Otology & Neurotology*; 2015 Sep; 36(8); 1343-1348. PMID: 26176556.

Wanna GB, Noble JH, Carlson ML, **Gifford RH**, **Dietrich MS**, Haynes DS, Dawant BM, Labadie RF. Impact of electrode design and surgical approach on scalar location and cochlear implant outcomes. *The Laryngoscope*; 2014 Nov; 124(S6); S1-S7. PMCID: PMC4209201.

The goal of this proposed research is to expand the evaluation of IGCIP in the pediatric population to effects on auditory function, speech understanding, language abilities, speech production, and literacy outcomes. My role in this research will be to advise and collaborate on all data management and statistical considerations, conduct statistical analyses as necessary, and to substantially participate in activities related to the dissemination of the findings from this research, as well as the development of research proposals based on these findings. I am currently Co-I on multiple NIH-funded studies. As is evident in my contributions to science and in my on-going/completed research support, these collaborations have been successful and productive.

## B. POSITIONS AND HONORS

**Positions and Employment**

| | |
|---|---|
| 1984-1989 | Statistical Consultant/Data Analyst, Center of Excellence, TN State University, Nashville, TN |
| 1986-2004 | Statistician, Instructional & Research Support, Vanderbilt University Information Technology Services, Nashville, TN |
| 1998- | Adjunct Faculty, College of Health Sciences, Belmont University, Nashville, TN |

| | |
|---|---|
| 2002- | Professor, Statistics & Measurement (Secondary Appt), Department of Psychiatry, School of Medicine, Vanderbilt University, Nashville, TN |
| 2004-2006 | Director, Education and Outreach, Vanderbilt Advanced Computing Center for Research and Education, Nashville, TN |
| 2006- | Professor, Biostatistics & Vanderbilt Ingram Cancer Center, School of Medicine, Vanderbilt University, Nashville, TN |
| 2006- | Professor, Statistics & Measurement, School of Nursing, Vanderbilt University, Nashville, TN |
| 2008-2014 | Senior Biostatistical Consultant/Co-Education Director, The Eunice Kennedy Shriver Intellectual, and Human Development Disability Research Ctr., Nashville, TN |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 1993- | Member, American Statistical Association |
| 2008- | Member, Eastern North American Region / International Biometric Society |

**Honors**

| | |
|---|---|
| 1996 | Hardy C. Wilcoxon Award, Most Distinguished Doctoral Dissertation in any area of psychological inquiry, Dept. of Psychology & Human Development, Vanderbilt University |
| 2008 | Dean's Award, Recognition of Faculty Achievement in Scholarly Endeavors, School of Nursing, Vanderbilt University |
| 2014 | Dean's Award, Recognition of Faculty Achievement in Research Endeavors, School of Nursing, Vanderbilt University |
| 2015 | Dean Colleen Conway-Welch Award for contributions to student learning, mentoring, modeling of professional behaviors, and encouragement of scholarship (Vanderbilt U. School of Nursing) |
| 2016 | Professional Research Recognition Award, Child Life Council |
| 2017 | Dean Colleen Conway-Welch Award for contributions to student learning, mentoring, modeling of professional behaviors, and encouragement of scholarship (Vanderbilt U. School of Nursing) |

## C. Contribution to Science

As a co-investigator with expertise in both statistics and measurement, my contributions to science could be organized a number of different ways. As demonstrated by my other support documentation, I am currently CO-I on multiple NIH-funded studies. My contributions to science listed below, as well as my complete bibliography online, demonstrate that my collaborations have been productive.

1. I have collaborated with researchers in psycho-neuroimaging (primarily fMRI) for more than 10 years. As those imaging methods have matured, I have facilitated the incorporation of cognitive and other self-report measures into the analyses of signal change measures (e.g., BOLD percent signal change).

    a. Monroe TB, Gibson SJ, Bruehl SP, Gore JC, **Dietrich MS**, Newhouse P, Atalla S, Cowan RL. Contact heat sensitivity and reports of unpleasantness in communicative people with mild to moderate cognitive impairment in Alzheimer's disease: a cross-sectional study. *BMC Medicine*, 2016 May; 14:74
    b. Monroe TB Beach PA, Bruehl SP, **Dietrich MS**, Rogers BP, Gore JC, Atalla SW, Cowan RL. The impact of Alzheimer's disease on the resting state functional connectivity of brain regions modulating pain: A cross sectional study. *Journal of Alzheimer's Disease*; 2017 Mar; 57(1); 71-83. PMID: 28222526.
    c. Atalia S, Gore J, Bruelh S, Rogers B, **Dietrich MS**, Benningfield M, Cowan R, Monroe T. BMI associated sex differences in pain reports and resting state functional connectivity in older adults. *Journal of Pain*; 2016 April; 17(4S); S59. PMID: 28162571.
    d. Monroe TB, Fillingim RB, Bruehl SP, Rogers BP, **Dietrich MS**, Gore JC, Atalla SW, Cowan RL. Sex Differences in Brain Regions Modulating Pain: A Cross Sectional Resting State Functional Connectivity Study. *Pain Medicine*; 2017 May 13; [Epub ahead of print]. PMID: 28505337.

2. Evidence of successful management and integration of data collected from large multi-site, multi-PI collaborative projects as well as statistical expertise related to appropriately conducting and analyzing data collected from clinical trials:

a. Sohl SJ, **Dietrich MS**, Wallston KA, Ridner SH. A randomized controlled trial of expressive writing in breast cancer survivors with lymphedema. *Psychology and Health*; 2017 Jul; 32(7); 826-842. PMID: 28355890
b. Lutenbacher M, Gabbe PT, Karp SM, **Dietrich MS**, Narrigan D, Carpenter L, Walsh W. Does additional prenatal care in the home improve birth outcomes for women with a prior preterm delivery? A randomized clinical trial. Matern Child Health J. 2014 Jul;18(5):1142-54. PubMed PMID: 23922160.
c. FitzHenry F, Wells N, Slater V, **Dietrich MS**, Wisawatapnimit P, Chakravarthy AB. A randomized placebo-controlled pilot study of the impact of healing touch on fatigue in breast cancer patients undergoing radiation therapy. Integr Cancer Ther. 2014 Mar;13(2):105-13. PubMed PMID: 24105358.
d. Ridner SH, Poage-Hooper E, Kanar C, Doersam JK, Bond SM, **Dietrich MS**. A pilot randomized trial evaluating low-level laser therapy as an alternative treatment to manual lymphatic drainage for breast cancer-related lymphedema. Oncol Nurs Forum. 2013 Jul;40(4):383-93. PubMed PMID: 23803270; PubMed Central PMCID: PMC3887507.

3. The application of my expertise in multiple domains of measurement methods (e.g., development and validation of self-report measures, assessment of possible screening measures, use and validation of physiological measures) is evidenced by the subset of manuscripts below.

a. Dillon NP, Kratchman LB, **Dietrich MS**, Labadie RF, Webster RJ 3rd, Withrow TJ. An experimental evaluation of the force requirements for robotic mastoidectomy. Otol Neurotol. 2013 Sep;34(7):e93-102. PubMed PMID: 23787968; PubMed Central PMCID: PMC3761064.
b. Ridner SH, Bonner CM, Doersam JK, Rhoten BA, Schultze B, **Dietrich MS**. Bioelectrical impedance self-measurement protocol development and daily variation between healthy volunteers and breast cancer survivors with lymphedema. Lymphat Res Biol. 2014 Mar;12(1):2-9. PubMed PMID: 24502422; PubMed Central PMCID: PMC3961792.
c. Young CC, **Dietrich MS**. Screening for rumination and brooding may be a feasible method of identifying adolescents at high risk for depression. J Pediatr Nurs. 2014 Nov-Dec;29(6):688-95. PubMed PMID: 24950241.
d. Ridner SH, **Dietrich MS**. Development and validation of the Lymphedema Symptom and Intensity Survey-Arm. Support Care Cancer. 2015 Oct; 23(10), 3103-3112. PMID: 25752884; PMCID: PMC4554806.

4. Novel application of statistical methods commonly used in disciplines outside of medicine and nursing to biomedical research. The work referenced below primarily focused on the application of group-based trajectory modeling from psychosocial research to biomedical research

a. Anderson CB, Kaufman MR, **Dietrich MS**, Barocas DA, Chang SS, Cookson MS, Smith JA Jr, Clark PE, Herrell SD. Recovery of urinary function after radical prostatectomy: identification of trajectory cluster groups. J Urol. 2012 Apr;187(4):1346-51. PubMed PMID: 22341278.
b. Ridner SH, **Dietrich MS**, Niermann K, Cmelak A, Mannion K, Murphy BA. A prospective study of the lymphedema and fibrosis continuum in patients with head and neck cancer. *Lymphatic Research and Biology*, 2016 Dec; 14(4), 198-205. PMID: 27305456.
c. **Role: Co-I** 1R01DE024982-01 (Deng) NIH/NIDCR 03/01/2015-02/28/2019
Establishing Lymphedema and Fibrosis Measures in Oral Cancer Patients
Determining reliability and validity of a patient-reported outcome measure, clinician-reported outcome measures, and imaging techniques (CT scan and ultrasonography) for assessing lymphedema and fibrosis in oral cavity and oropharyngeal cancer patients across the trajectory of treatment, recovery, and survival
d. Neal JL, Lowe NK, Phillippi JC, Ryan SL, Knupp AM, **Dietrich MS**, Thung SF. Likelihood of cesarean delivery after applying leading active labor diagnostic guidelines. *Birth*; 2017 Jun; 44(2); 128-136. PMID: 28198038.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/1BCXkivlxwqQc/bibliography/47517739/public/?sort=date&direction=descending

**D. Research Support (Ongoing Research Support)**

[redacted]

R01DC008408 (Dawant) NIH/NIDCD / sub: VUMC: (Labadie) 07/01/2016-06/30/2018
Clinical Validation and Testing of Percutaneous Cochlear Implantation
Continues to build on our successful development of PCI and explore potential benefits by (i) extending our Phase I study by one year in order to produce a robust clinical protocol and (ii) carrying out a Phase II study consisting of a randomized clinical trial comparing PCI to traditional CI surgery.

1R01DE024982-01 (Deng) NIH/NIDCR 04/01/2015-03/31/2019
Establishing Lymphedema and Fibrosis Measures in Oral Cancer Patients
Determining reliability and validity of a patient-reported outcome measure, clinician-reported outcome measures, and imaging techniques (CT scan and ultrasonography) for assessing lymphedema and fibrosis in oral cavity and oropharyngeal cancer patients across the trajectory of treatment, recovery, and survival

1R01NR015353-02 (Akard) NIH/NINR 09/26/2014-06/30/2018
Impact of a PCRC-Supported Legacy Intervention in Pediatric Palliative Care
Leveraging resources from the PCRC and contribute back to the greater body of palliative care and end of life knowledge promoted by the PCRC.

[redacted]

2P30 CA068485-19 (Pietenpol) NIH/NCI 09/05/1995-08/31/2020
Cancer Center Support Grant
Conduct, coordinate, and integrate the cancer-related activities of Vanderbilt University.

**Completed Research Support (**Completed in **past 3 years** from **32** completed**)**

1R21AG050483-A01A (Sarkar) NIH/NIA 08/15/2016-04/30/2018
Socially Assistive Robotic Architecture for Elder Care
Continues the development of an innovative socially assistive robotic framework in addressing the needs of older adults examining the feasibility for use in the community, assisted living and nursing home, and examine older adults' acceptance and tolerance.

1R21EB015623-01A1 (Simaan) NIBIB 07/01/2013-06/30/2017
Dexterous Robot-Assisted Trans-Urethral Bladder Resection
Enabling higher precision, safer, and more dexterous resection and surveillance of bladder tumors.

1DP3DK097706-01 (Mulvaney) NIH/NIDCD 0 9/21/2012-12/31/2016
Using Social Learning to Improve Adolescent Diabetes Adherence Problem Solving
Integrating social interactions with peers with skill building activities to improve diabetes control adherence in the adolescent population.

5R01 DC008408-05A1 (Labadie) NIH/NIDCD 07/13/2012-06/30/2016
Clinical Validation and Testing of Percutaneous Cochlear Implantation
Investigation of less invasive cochlear access by using image guided surgical (IGS) techniques (adults).

[redacted]

1R21AG045735-01A1 (Monroe) NIH/NIA 04/01/2014-06/30/2016
Age-related Differences in Psychophysical and Neurobiological Response to Pain
Compare pain processing in a broad range of adults (ages 30-89)with the goal of providing a foundation for developing improved pain treatment methods for older adults.

5 R21 DA033341 (Cowan) NIDA 01/15/2013-1/14/2016
Neural Mechanisms of Increased Cortical Excitability in Human MDMA/Ecstasy Users
Use of several neuroimaging methods to further understand how MDMA use damages the brain and how we might eventually develop treatments for people with MDMA-induced brain damage.

1R21MH101321-01A1 (Cascio) NIMH 03/07/2014-10/31/2015
Mapping Thalamocortical Networks across Development in ASD
Contribute to our understanding of the brain-basis of ASD and provide useful biomarkers that will further our understanding of the etiology of ASD and contribute to the development of new treatments.

R21CA173202-1A1 (Ridner) NIH/NCI 07/01/2013-07/31/2015
Feasibility and Preliminary Efficacy of Yoga in Head and Neck Cancer Survivors
Tailoring Yoga techniques to address musculoskeletal impairment (MSI) of the neck, shoulder, and jaw, as well as postural abnormalities in head and neck cancer survivors.

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Nittrouer, Susan

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor and Chair

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| West Chester State College, West Chester, PA | B.S. | 06/1974 | Education, Speech Pathology |
| Smith College, Northampton, MA | M.E.D. | 06/1975 | Education of the Deaf |
| City University of New York, New York, NY | Ph.D. | 07/1985 | Speech and Hearing Sciences |
| Haskins Laboratories, New Haven, CT | Postdoctoral Fellowship | 02/1987 | Speech Science |

**A. Personal Statement**

Work in my laboratory focuses on how listeners manage to recover linguistically significant and stable representations from the acoustic speech signal, which is highly variable. My interests have largely involved the development of speech perception abilities, and investigations in my laboratory have included typically developing children, in order to extend our understanding of how this process normally unfolds. Nonetheless, two additional populations in which I have been especially interested are children with hearing loss and children with phonologically based dyslexia. The goal is to explore why these children face particular challenges in this process of discovering phonological structure in the acoustic speech signal; syntactic competencies remain relatively intact.

The work proposed on this grant titled *Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy* is commensurate with my interests because proposed procedures could improve the quality of the signal available to children with cochlear implants. Presumably, these children suffer language deficits – especially in the phonological domain – because of degraded auditory signals. Improving the signal should improve their acquisition of sensitivity to phonological structure, which should have cascading effects on the learning of other language skills.

**Nittrouer, S.** (2006) Children hear the forest. ***J. Acoust. Soc. Am. 120****,* 1799-1802***.*** PMCID: PMC1994091

**Nittrouer, S.** & Pennington, B.F. (2010). New approaches to the study of childhood language disorders. ***Current Directions in Psychological Science 19,*** 308-313. PMCID: PMC3374334

**Nittrouer, S.** (2012). A new perspective on developmental language problems: Perceptual organization deficits. ***Perspective on Language Learning & Education, 19***, 87-97. PMCID: PMC3749876

**Nittrouer, S.** & Lowenstein, J.H. (2014). Separating the effects of acoustic and phonetic factors in linguistic processing by adults and children. ***Appl. Psycholinguist. 35*****,** 333-370. PMCID: PMC3981461

**B. Positions and Honors.**

**Positions and Employment**

1975-1976 Middle School Teacher, Clarke School for the Deaf, Northampton, MA
1976-1978 Preschool Teacher, Montreal Oral School for the Deaf, Montreal, Quebec
1978-1979 Speech Coordinator, Beverly School for the Deaf, Beverly, MA
1979-1980 Speech Coordinator, The Learning Center for Deaf Children, Framingham, MA
1980-1982 Graduate Student, Psychology, Utah State University, Logan, UT
1981-1982 Teaching Assistant for Graduate Statistics Classes, Utah State University, Logan, UT
1982-1985 Graduate Student, Speech and Hearing Sciences, City University of New York Graduate School, New York, NY (Advisor: M Studdert-Kennedy)

1982-1983 Coordinator, Inservice Training Project on Teaching Speech to the Hearing-Impaired, City University of New York Graduate School, New York, NY (PI: I Hochberg)
1983-1985 Research Assistant on a project examining the contributions to speech perception of "top-down" phonotactic and sentential context, CUNY Graduate School, New York, NY (PI: A Boothroyd)
1985-1987 NIH Postdoctoral Fellow, Haskins Laboratories, New Haven, CT (Mentors: S Kelso, T Baer, K Harris)
1987-1990 Staff Scientist, Boys Town National Research Hospital (BTNRH), Omaha, NE
1987-1990 Assistant Professor, Dept. of Otolaryngology and Human Communication, Creighton University School of Medicine, Omaha, NE
1990-1993 Associate Professor, University of Nebraska at Omaha, Omaha, NE
1993-2002 Staff Scientist, Boys Town National Research Hospital (BTNRH), Omaha, NE
1993-1999 Associate Professor, Dept. of Otolaryngology & Human Communication, Creighton University School of Medicine, Omaha, NE
1999-2002 Professor, Dept. of Otolaryngology and Human Communication, Creighton University School of Medicine, Omaha, NE
2002-2005 Director, Division of Exemplary Services, Center for Persons with Disabilities, Utah State University, Logan, UT
2002-2005 Professor, Dept. of Communicative Disorders, Utah State University, Logan, UT
2005-2015 Professor, Speech and Hearing Science, Ohio State University, Columbus, OH
2007-2015 Professor and Director of Research, Otolaryngology, Ohio State University, Columbus, OH
2015-present Professor and Chair, Speech, Language, and Hearing Sciences, University of Florida, Gainesville, FL

**Other Experience and Professional Memberships**

1991-1992 Member, NIDCD *ad hoc* committee for the review of small grant proposals
1992-2000 Member, Acoustical Society Technical Committee on Speech Communication
1994-1996 *Ad hoc* member, Sensory Disorders and Language Study Section
1997-1998 Associate Editor, speech, *Journal of Speech, Language, and Hearing Research*
2002-2005 Associate Editor, *Volta Review*
2003-2005 Associate Editor, language, *Journal of Speech, Language, and Hearing Research*
2005 Member of organizing committee, Hearing Loss in Children: Rehabilitation and Education Issues, American Speech-Language-Hearing Convention
2010 Chair of organizing committee for early intervention for deaf children special session, American Speech-Language-Hearing Convention
Ongoing Reviewer for various NIDCD and LCOM study sections
2011-present Associate Editor, *International Journal of Audiology*
2012-2015 Member, Academic Affairs Board, American Speech, Language, Hearing Association

**Honors**

1989 Editors' Award for best paper in speech, *Journal of Speech and Hearing Research*
1996 Editors' Award for best paper in hearing, *Journal of Speech and Hearing Research*
2009 Fellow, Acoustical Society of America
2013 Editor's Award for best paper in hearing. *Journal of Speech, Language, and Hearing Research*

## C. Contribution to Science

*C.1. Developmental Weighting Shift*

The prevailing wisdom among speech perception researchers in the latter half of the 20th century was that human listeners collect discrete pieces of the spectrotemporal structure from the speech signal, termed acoustic cues, and directly map the values of those cues to phonemic categories. The major experimental paradigm utilized in that work involved categorical perception experiments, in which all structure of simple (usually CV) syllables remained constant across a set, except one. That one cue would be manipulated to span values from one appropriate for one phonemic category to one appropriate for another. Results revealed a range of cue settings that signaled the phoneme represented at each end of the continuum. In 1980, Mann and Repp demonstrated a phenomenon they termed "trading relations" in which they showed that if two cues were manipulated in an experiment, the value of one cue required to signal a specific phonemic category varied depending on the setting of another cue. In particular, the value of a relatively stationary cue – such as the spectral shape of a fricative noise – signaling a specific sibilant varied depending on the structure of formant transitions at voicing onset. But that dynamic cue – the formant transitions – was viewed as "secondary," meaning it was thought that adults had learned over childhood how formant transitions covary with the "primary" cue, which was thought to be the fricative-noise spectrum. My dissertation research was designed to track the developmental course of learning about the presumed secondary cue, so the emergence of trading relations. But things did not go as expected. No matter how I constructed my stimuli, children always showed a stronger effect of the supposed secondary

cue, the formant-transitions, than adults. And the attention – or weight – given to that cue diminished with increasing age, while the weight given to the noise spectrum increased. Thus the notion of a developmental weighting shift was born, and future studies supported the idea. At the same time, other investigators were reporting that the perceptual weights given to various cues were language specific, meaning they varied across languages. Thus the developmental weighting shift was determined to depend on experience with a first language, rather than simply to unfold across childhood, irrespective of input.

**Nittrouer, S.** (1992). Age-related differences in perceptual effects of formant transitions within syllables and across syllable boundaries. ***J. Phonet. 20,*** 351-382.

**Nittrouer, S.**, Manning, C. & Meyer, G. (1993). The perceptual weighting of acoustic cues changes with linguistic experience. ***J. Acoust. Soc. Am. 94,*** S1865.

**Nittrouer, S.** & Miller, M.E. (1997). Predicting developmental shifts in perceptual weighting schemes. ***J. Acoust. Soc. Am. 101,*** 2253-2266. PMID: 9104027

**Nittrouer, S.** (2004). The role of temporal and dynamic signal components in the perception of syllable-final stop voicing by children and adults. ***J. Acoust. Soc. Am. 115***, 1777-1790. PMCID: PMC1994085

*C.2. Perceptual organization and speech perception*

The work described above helped move theoretical models of speech perception (so of how listeners recover phonemic structure from the acoustic speech signal) away from passive ones suggesting acoustic cues are simply harvested, and values compared against a menu of cue-to-phoneme translations. It was becoming clear that perceptual/cognitive processes were involved; although the point where perceptual gives way to cognitive is hard to assign. At the same time it was being demonstrated by other investigators that listeners are able to recognize speech, especially when presented at sentence length, when acoustic cues are almost completely eliminated. This was accomplished with the use of sine-wave analogs and noise-vocoded stimuli. Thus more evidence was accumulating to support the idea that listening to speech entails active mechanisms that guide what sensory inputs are attended to and how they are organized. Although this phenomenon of perceptual organization is best assessed when sensory inputs are degraded (think of the simple line drawings of the Ruben vase that can be organized as two profiles or one vase), we actively organize sensory inputs in all of perception. Work in our laboratory helped to establish a few effects related to perceptual organization for speech signals. ***(1)*** The way these signals are organized is apparently language specific, just like perceptual weighting strategies. This was demonstrated when it was observed that even highly proficient second-language learners (adults) of English are poorer than native speakers at recognizing signals such as noise-vocoded and sine-wave speech. ***(2)*** Children acquire the perceptual organization strategies that are optimal for their native language through language experience. This was demonstrated when it was observed that recognition of noise-vocoded and sine-wave speech improves as children get older, and so gain language experience. ***(3)*** Children learn to organize dynamic spectral structure associated with speech production sooner than they learn to organize signals lacking in that kind of structure. This was demonstrated when it was observed that by age 7 years children recognize sine wave speech as well as adults, but continue to perform more poorly with noise-vocoded signals, at least up to eight-channels. (Some studies on perception of noise-vocoded signals by adults and children have interpreted the age-related difference observed in these studies as indicating that children need more channels of information. While strictly accurate, we interpret the poorer recognition of children than of adults for equivalent numbers of noise-vocoded channels as evidence of their immature perceptual organization.) ***(4)*** Development of perceptual organization for speech is delayed for children with normal hearing who have language-learning deficits, such as dyslexia: Children with dyslexia are poorer at recognition of noise-vocoded speech than their peers with normal reading development.

**Nittrouer, S.**, Lowenstein, J.H., & Packer, R. (2009). Children discover the spectral skeletons in their native language before the amplitude envelopes. ***J. Exp. Psych.: Human Percep. and Perf. 35,*** 1245-1253. PMCID: PMC3307092

**Nittrouer, S.** & Lowenstein, J. H. (2010). Learning to perceptually organize speech signals in native fashion. ***J. Acoust. Soc. Am. 127,*** 1624-1635. PMCID: PMC2856515

**Nittrouer, S.** & Lowenstein, J.H. (2013). Perceptual organization of speech signals by children with and without dyslexia. ***Res. Dev. Disabil. 34,*** 2304-2325. PMCID: PMC3674161

**Nittrouer, S.,** Lowenstein, J. H., Wucinich, T. & Tarr, E. (2014). Benefits of preserving stationary and time-varying formant structure in alternative representations of speech: Implications for cochlear implants. ***J. Acoust. Soc. Am. 136,*** 1845-1856. PMCID: PMC4223981

*C.3. Combining electric stimulation with even a little acoustic stimulation enhances language learning*

Work in my laboratory has investigated ways to enhance the acoustic speech signal to permit better recognition, within the limits imposed by hearing loss. One earlier and unexpected outcome of our work was that we found that children with cochlear implants (CIs) who had continued using a hearing aid after receiving a first CI were performing better on language measures than the children who discontinued using a hearing aid. This was the case, in spite of other relevant factors such as socioeconomic status, age of receiving that first CI, and amount of residual hearing prior to implantation. This finding led us to explore the phenomenon in more depth, asking if a very low-frequency signal is beneficial to speech perception with degraded signals in the spectral range typically provided by auditory prostheses.

**Nittrouer, S.** & Chapman, C. (2009). The effects of bilateral electric and bimodal electric-acoustic stimulation on language development. ***Trends in Amplification, 13,*** 190-205. PMCID: PMC3271432

**Nittrouer, S.**, Caldwell, A. Lowenstein, J. H., Tarr, E., & Holloman, C. (2012). Emergent literacy skills in kindergartners with cochlear implants. ***Ear & Hearing, 33,*** 683-697. PMCID: PMC3419773

**Nittrouer, S.**, Tarr, E., Bolster, V., Caldwell-Tarr, A., Moberly, A.C., & Lowenstein, J.H. (2014). Very low-frequency signals support perceptual organization of implant-simulated speech for adults and children. *International Journal of Audiology. 53*, 270-284. PMCID: PMC3954900

Moberly, A.C., Lowenstein, J.H., & **Nittrouer, S.** (2016) Early bimodal stimulation benefits language acquisition for children with cochlear implants. ***Otology & Neurotology, 37,*** 24-30. PMCID: PMC4675676

*C.4. The development of mature speech perception strategies depends on more than just auditory sensitivity to acoustic cues*

Research in this laboratory has shown that the acquisition of sensitivity to phonological (especially phonemic) structure by children is an event that unfolds over a protracted period of time; infants are not born being able to recognize phonemic segments, and they do not learn to do so early in life. That conclusion makes sense, in light of the fact that recovering phonemic structure in one's native language does not rest solely on having sensitivity to the acoustic cues underlying phonemic categories. Although it is critically important to have access to as much signal detail as possible (making bimodal stimulation advantageous), there is more to speech recognition. Appropriate attentional and organizational strategies are required. Evidence for that assertion comes from studies showing that listeners are able to recognize speech when acoustic cues are almost completely eliminated. This finding has been demonstrated with sine-wave analogs and noise-vocoded stimuli. Thus listening to speech entails active mechanisms that guide what sensory inputs are attended to, and how they are organized. It takes time for children to develop these skills. We know these mechanisms are critical to language acquisition because the development of language-specific attentional and organizational strategies for speech is delayed for children with normal hearing who have language-learning deficits, such as dyslexia: For example, children with dyslexia are poorer at recognition of noise-vocoded speech than their peers with normal reading development. It is precisely the fact that these kinds of organizational strategies are involved in speech perception that makes recognition with a CI possible; if speech recognition depended exclusively on having access to specific acoustic cues, it likely would be much poorer for listeners with CIs than what we observe. Consequently understanding how children acquire the appropriate attentional and organizational strategies for speech is important to understanding spoken language development in deaf children, especially those who use CIs.

**Nittrouer, S.** (1996). Discriminability and perceptual weighting of some acoustic cues to speech perception by three-year-olds. ***J. Speech Hear. Res. 39***, 278-297.

**Nittrouer, S.** & Crowther, C.S. (1998). Examining the role of auditory sensitivity in the developmental weighting shift. ***J. Speech Lang. Hear. Res. 41***, 809-818. PMID: 9712128

**Nittrouer, S.** (1999). Do temporal processing deficits cause phonological processing problems? ***J. Speech Lang. Hear. Res. 42***, 925-942. PMID:10450912

**Nittrouer, S.**, & Lowenstein, J.H. (2007). Children's weighting strategies for word-final stop voicing are not explained by auditory capacities. ***J. Speech Lang. Hear. Res. 50,*** 58-73. PMCID: PMC1994088

**Full bibliographic resource can be found at:** *http://www.ncbi.nlm.nih.gov/pubmed/?term=nittrouer+s*

**D. Current Research Support.**

**R01 DC015992** Nittrouer (PI) 03/01/2017-02/28/2020
NIH-NIDCD
Spoken Language in Adolescents with Hearing Loss
This is part of a longitudinal project designed to examine outcomes in children born with moderate-to-profound hearing loss.

**E. Research Support within the past 3 years.**

**R01 DC000633** Nittrouer (PI) 12/01/88-06/30/17
NIH-NIDCD
*Ontogeny of Segmental Speech Organization*
The long-term goal of this project is to develop a theoretical account of how children acquire access to the segmental structure of speech.

**R01 DC006237** Nittrouer (PI) 09/01/03-08/31/16
NIH-NIDCD
*Early Development of Children with Hearing Loss*
The long-term goal of this project was to understand the factors that contribute to the development of spoken language, cognition, and psychosocial wellbeing in children with hearing loss.

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ferenc Bunta

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Associate Professor of Communication Sciences and Disorders

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Lajos Kossuth University, Debrecen, Hungary | B.Ed. | 06/1994 | TESL |
| Arizona State University, Tempe, AZ | M.A. | 05/1999 | Linguistics |
| Arizona State University, Tempe, AZ | Ph.D. | 08/2005 | Speech & Hearing Science |
| Temple University, Philadelphia, PA | Postdoctoral | 05/2008 | Communication Sciences & Disorders |

### A. Personal Statement

I have expertise directly relevant for the proposed project (specifically, Aims 2 and 3), and I am glad to assist Dr. Gifford to successfully complete the research project as her consultant. I have conducted research on bilingual and monolingual speech and language acquisition throughout my academic career with a recent focus on phonological development in children with hearing loss who use cochlear implants; work funded in part by the NIH/NIDCD. Aim 2 of the proposed project is on speech and language outcomes in pediatric cochlear implant (CI) users; an area on which my research directly focuses, evidenced by my publication record. I use techniques (such as acoustic analyses and other phonological measures) proposed by Dr. Gifford, so my expertise are directly relevant. Regarding Aim 3, I have also published in the area of language outcomes as well as phonological awareness in bilingual and monolingual children, so a combination with my expertise in phonological acquisition, speech and language outcomes, and how those are related to phonological awareness in CI users will benefit Dr. Gifford's project. I have also had the privilege of collaborating with Dr. Gifford on a paper we published on *Dual language versus English only support for bilingual children with hearing loss who use cochlear implants and hearing aids* listed below that is not only relevant to this project, but it also provides evidence of our professional collaborative relationship. I am enthusiastic about supporting Dr. Gifford's proposed project as a consultant, and I am looking forward to our collaboration on this research as well as providing my expertise to the project.

My publications most relevant for the present project include:

a) Li, F., Bunta, F., & Tomblin, J. B. (2017). Alveolar and postalveolar voiceless fricative and affricate productions of Spanish-English bilingual children with cochlear implants. *Journal of Speech, Language, and Hearing Research, 60*, 2427-2441. doi:10.1044/2017_JSLHR-S-16-0125
b) Bunta, F., Goodin-Mayeda, C. E., Procter, A., & Hernandez, A. (2016). Initial stop voicing in bilingual children with cochlear implants and their peers with normal hearing. *Journal of Speech, Language, and Hearing Research, 59*, 686-698. doi:10.1044/2016_JSLHR-S-15-0212
c) Bunta, F., Douglas, M., Dickson, H., Cantu, A., Wickesberg, J., & Gifford, R. H., (2016). Dual language versus English only support for bilingual children with hearing loss who use cochlear implants and hearing aids. *International Journal of Language and Communication Disorders, 51*(4), 460-472. doi: 10.1111/1460-6984.12223

d) Bunta, F., & Douglas, M. (2013). The effects of dual language support on the English language skills of bilingual children with cochlear implants and hearing aids as compared to monolingual peers. *Language, Speech and Hearing Services in Schools, 44*, 281-290. doi: 10.1044/0161-1461(2013/12-0073)

## B. Positions and Honors

2005-2008 Postdoctoral Research Fellow, Department of Communication Sciences and Disorders, Temple University, Philadelphia, PA
2008-2014 Assistant Professor, Department of Communication Sciences and Disorders, The University of Houston, Houston, TX
2014-present Associate Professor, Department of Communication Sciences and Disorders, The University of Houston, Houston, TX

**Other Experience and Professional Memberships**

2017-present Editorial Board member for *Journal of Speech, Language, and Hearing Research* and *Beszédkutatás*

2015 Peer Reviewer for American Speech-Language-Hearing Association (New Century Scholars grant panel)

2014 Reviewer for American Speech-Language-Hearing Association (Advancing Academic Research Careers, Students Preparing for Academic & Research Careers Grant, ad-hoc)

2012-present Member, International Expert Panel on Multilingual Children's Speech

2010-present Member, International Clinical Phonetics and Linguistics Association
2009-2010 Peer Reviewer for NSF (ad-hoc)
2004-present Peer Reviewer for over 20 scholarly journals (e.g., *Applied Psycholinguistics, American Journal of Speech-Language Pathology*, etc.)

**Academic and Professional Honors**

1999-2002 University Graduate Fellows, Arizona State University (ASU)
2003 Student Affairs' Tribute to University Staff for excellence in teaching and student mentoring, ASU,
2003-2004 Spencer Fellow, The Spencer Foundation
2004 Fifteenth Annual Student Affairs' Tribute to Faculty and Academic Professionals, ASU

## C. Contributions to Science

1. One of my current lines of work is on phonological skills of bilingual and monolingual children with hearing loss who use CIs (funded by the NIDCD/NIH, R03DC012640 from 2013 through 2017). This innovative research provides novel insights into both theory and clinical practice, because it represents the intersection of speech and language acquisition in bilinguals who have a diminished auditory signal and the population is one that is in critical need of information for educators and practicing speech-language pathologists. This research is directly relevant for the proposed project (as detailed in the **Personal Statement** section above), because it includes speech analyses (including acoustic measures and phonological analyses), some of which are also used in the present proposal. Relevant peer-reviewed publications are listed in the **Personal Statement** section above.

2. As part of an interdisciplinary team of researchers across multiple sites (University of Houston and University of Texas at Dallas), I am currently also a co-investigator on a current grant by the US Department of Education (R324A160258). I provide my expertise in phonology and speech development as a co-investigator of a project whose goal is to develop guidelines for the identification and classification of Spanish-speaking English Learners (ELs) who are at-risk of developing significant learning disabilities in reading, language, or both. This project is also directly relevant to the current application, because they both include investigations of

the effects of phonological awareness on other language measures. A selection of my representative publications on this topic are:

a) Rojas, R., Iglesias, A., Bunta, F., Goldstein, B., Goldenberg, C., & Reese, L. (2015). Interlocutor differential effects on the expressive language skills of Spanish-speaking English learners. *International Journal of Speech-Language Pathology.* doi: 10.3109/17549507.2015.1081290.
b) Branum-Martin, L, Tao, S., Garnaat, S., Bunta, F., & Francis, D. J. (2012). Meta-analysis of bilingual phonological awareness: Language, age, and psycholinguistic grain size. *Journal of Educational Psychology, 104*(4), 932-944. doi: 10.1037/a0027755
c) Major, R. C., Fitzmaurice, S., Bunta, F., & Balasubramanian (2002). The effects of nonnative accents on listening comprehension: Implications for ESL assessment. *TESOL Quarterly, 36,* 173-190.

3. I transitioned from linguistics and second language phonology to speech and hearing sciences for my doctoral studies, and therefore, my work expanded to include bilingual and cross-linguistic phonological acquisition in children with typical speech and language development. My collaborators and I have made significant contributions to science in this area by conducting a series of studies using various techniques from acoustic analyses to traditional phonological and speech measures. Some of our work on phonological whole-word measures was novel and has since received recognition. The eclectic approach to analyzing speech allowed me to address complex phonological problems from various angles that will benefit Dr. Gifford's project. A selection of my representative publications on the topic are:

a) Bunta, F., Davidovich, I., & Ingram, D. (2006). The relationship between the phonological complexity of a bilingual child's words and those of the target languages. *International Journal of Bilingualism, 10* (1), 71-88.
b) Bunta, F., & Ingram, D. (2007). The acquisition of speech rhythm by bilingual Spanish- and English-speaking four- and five-year-old children. *Journal of Speech, Language, and Hearing Research, 50* (4), 999-1014. doi:10.1044/1092-4388(2007/070).
c) Bunta, F., Fabiano, L., Ingram, D., & Goldstein, B. (2009). Phonological whole-word measures in three-year-old bilingual children and their monolingual peers. *Clinical Linguistics and Phonetics, 23*(2), 156-175.
d) Goldstein, B., & Bunta, F. (2012). Positive and negative transfer in the phonological systems of bilingual speakers. *The International Journal of Bilingualism, 16*(4), 388-401. doi:10.1177/1367006911425817.

4. My early work focused on second language phonology and foreign accents from a linguistic perspective. This line of work provided contributions to both the effects of non-native accents on listening comprehension and regarding the acquisition of specific phonemes that pose challenges to English as a second language learners. Listening comprehension is related to speech perception, so I will be able to provide my relevant expertise to the proposed project. A selection of my representative publications on the topic are:

a) Bunta, F., & Major, R. C. (2004). An Optimality Theoretic account of Hungarian ESL learners acquisition of /E/ and /Θ/. *International Review of Applied Linguistics in Language Teaching, 42,* 277-298. doi:10.1515/iral.2004.014.
b) Major, R. C., Fitzmaurice, S., Bunta, F., & Balasubramanian, C. (2005). Testing the effects of regional, ethnic, and international dialects of English on listening comprehension. *Language Learning, 55* (1), 37-69.
c) Major, R. C., Fitzmaurice, S., Bunta, F., & Balasubramanian (2002). The effects of nonnative accents on listening comprehension: Implications for ESL assessment. *TESOL Quarterly, 36,* 173-190.
d) Santos Oliveira, D., Casenhiser, D. M., Hedrick, M., Teixeira, A., & Bunta, F. (2016). Effects of language experience on the discrimination of the Portuguese palatal lateral by nonnative listeners. *Clinical Linguistics and Phonetics.* doi: 10.3109/02699206.2016.1152508.

**Partial List of Publications on PubMed**
http://www.ncbi.nlm.nih.gov/pubmed/?term=bunta%2C+ferenc

## D. Research Support

### Current Research Support

US Department of Education 08/01/16-07/31/18
(R324A160258)
Identification of reading and language disabilities in Spanish-speaking English learners
The goal of the project is to develop guidelines for the identification and classification of Spanish-speaking English Learners (ELs) who are at-risk of developing significant learning disabilities in reading, language, or both.
Role: Co-Investigator

[redacted]

### Completed Research Support

National Institute on Deafness and Other Communication Disorders/National Institutes of Health
(R03DC012640) 08/01/13-07/31/17
Phonological acquisition in bilingual children with cochlear implants
The goal of this research is to discover how bilingual children who use cochlear implants acquire the phonological systems of their target languages. Specifically, I will (1) investigate the effects of the diminished auditory signal on the speech of bilingual children with cochlear implants via comparisons to bilingual peers with normal hearing. I will also (2) examine cross-language effects by comparing the phonological skills of bilingual children with cochlear implants to those of their monolingual English-speaking peers with cochlear implants.
Role: PI

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 1

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Rene | H | Gifford | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2. | | Stephen | M | Camarata | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 3. | | Robert | F | Labadie | | Co-Investigator | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| 0 | Post Doctoral Associates | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Graduate Students | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Undergraduate Students | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Secretarial/Clerical | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Other | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Other Professionals | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Allocated Admin Support | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2 | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | [redacted] |
| 2. Foreign Travel Costs | [redacted] |
| **Total Travel Cost** | [redacted] |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | [redacted] |
| 2. Stipends | | [redacted] |
| 3. Travel | | [redacted] |
| 4. Subsistence | | [redacted] |
| 5. Other: Other | | [redacted] |
| **0 Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | [redacted] |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8 . Other Direct Costs | [redacted] |
| 9 . All Other Costs | [redacted] |
| **Total Other Direct Costs** | [redacted] |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC, Research On/ Off campus-Remote | [redacted] | [redacted] | [redacted] |
| | | **Total Indirect Costs** | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: M-19_S2S_Budget_Justification.pdf (Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Enter name of Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Rene | H | Gifford | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2 . | | Stephen | M | Camarata | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 3 . | | Robert | F | Labadie | | Co-Investigator | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| 0 | Post Doctoral Associates | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Graduate Students | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Undergraduate Students | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Secretarial/Clerical | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Other | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Other Professionals | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Allocated Admin Support | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| **2** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |

**Total Salary, Wages and Fringe Benefits (A+B)** [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | [redacted] |
| 2. Foreign Travel Costs | [redacted] |
| **Total Travel Cost** | [redacted] |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | [redacted] |
| 2. Stipends | | [redacted] |
| 3. Travel | | [redacted] |
| 4. Subsistence | | [redacted] |
| 5. Other: Other | | [redacted] |
| **0 Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | [redacted] |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8 . Other Direct Costs | [redacted] |
| 9 . All Other Costs | [redacted] |
| **Total Other Direct Costs** | [redacted] |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC, Research On/ Off campus-Remote | 58 | [redacted] | [redacted] |
| | | **Total Indirect Costs** | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

**L. Budget Justification*** File Name: M-19_S2S_Budget_Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS* [redacted]

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Rene | H | Gifford | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2. | | Stephen | M | Camarata | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 3. | | Robert | F | Labadie | | Co-Investigator | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| 0 | Post Doctoral Associates | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Graduate Students | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Undergraduate Students | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Secretarial/Clerical | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Other | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Other Professionals | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Allocated Admin Support | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2 | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | [redacted] |
| 2. Foreign Travel Costs | [redacted] |
| **Total Travel Cost** | [redacted] |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | [redacted] |
| 2. Stipends | | [redacted] |
| 3. Travel | | [redacted] |
| 4. Subsistence | | [redacted] |
| 5. Other: Other | | [redacted] |
| **0 Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | [redacted] |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8 . Other Direct Costs | [redacted] |
| 9 . All Other Costs | [redacted] |
| **Total Other Direct Costs** | [redacted] |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC, Research On/ Off campus-Remote | [redacted] | [redacted] | [redacted] |
| | | **Total Indirect Costs** | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: M-19_S2S_Budget_Justification.pdf (Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ● Project ○ Subaward/Consortium

**Enter name of Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | | Rene | H | Gifford | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2. | | Stephen | M | Camarata | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 3. | | Robert | F | Labadie | | Co-Investigator | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| 0 | Post Doctoral Associates | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Graduate Students | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Undergraduate Students | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Secretarial/Clerical | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Other | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Other Professionals | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Allocated Admin Support | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2 | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | [redacted] |
| 2. Foreign Travel Costs | [redacted] |
| **Total Travel Cost** | [redacted] |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | [redacted] |
| 2. Stipends | | [redacted] |
| 3. Travel | | [redacted] |
| 4. Subsistence | | [redacted] |
| 5. Other: Other | | [redacted] |
| **0 Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | [redacted] |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8 . Other Direct Costs | [redacted] |
| 9 . All Other Costs | [redacted] |
| **Total Other Direct Costs** | [redacted] |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC, Research On/ Off campus-Remote | [redacted] | [redacted] | [redacted] |
| | | **Total Indirect Costs** | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: M-19_S2S_Budget_Justification.pdf (Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Enter name of Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Rene | H | Gifford | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 2 . | | Stephen | M | Camarata | | PD/PI | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 3 . | | Robert | F | Labadie | | Co-Investigator | [redacted] | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| 0 | Post Doctoral Associates | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Graduate Students | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Undergraduate Students | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Secretarial/Clerical | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 1 | Other | [redacted] | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Other Professionals | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| 0 | Allocated Admin Support | 0 | 0 | 0 | [redacted] | [redacted] | [redacted] |
| **2** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |

**Total Salary, Wages and Fringe Benefits (A+B)** [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | [redacted] |
| 2. Foreign Travel Costs | [redacted] |
| **Total Travel Cost** | [redacted] |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | [redacted] |
| 2. Stipends | | [redacted] |
| 3. Travel | | [redacted] |
| 4. Subsistence | | [redacted] |
| 5. Other: Other | | [redacted] |
| **0 Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | [redacted] |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ● Project ❍ Subaward/Consortium

**Organization:** Vanderbilt University Medical Center

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8 . Other Direct Costs | [redacted] |
| 9 . All Other Costs | [redacted] |
| **Total Other Direct Costs** | [redacted] |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| **Total Direct Costs (A thru F)** | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC, Research On/ Off campus-Remote | [redacted] | [redacted] | [redacted] |
| | | **Total Indirect Costs** | [redacted] |

| | |
|---|---|
| **Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number) | Department of Health and Human Services , Steven Zuraf (301) 492-4855 |

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| **Total Direct and Indirect Institutional Costs (G + H)** | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | |
|---|---|
| | File Name: M-19_S2S_Budget_Justification.pdf (Only attach one file.) |

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# DETAILED BUDGET JUSTIFICATION

## PRINCIPAL INVESTIGATORS

### Multi-PI: René H. Gifford, PhD, CCC-A

[redacted] calendar months in Years 1-5

As the director of the Cochlear Implant Program at the Vanderbilt Bill Wilkerson Center, Dr. Gifford will be critical in the recruitment of study participants as well as CI programming as she is one of 3 study members who will be familiar with the randomization. She will prepare the data for analysis as well as for written and oral presentation and oversee study personnel including the project manager and PhD student.

### Multi-PI: Stephen Camarata, PhD, CCC-SLP

[redacted] calendar months in Years 1-5

Dr. Camarata will train all experimenters involved in the developmental assessments, including language, literacy and achievement assessments. In addition, he will prepare these data (i.e., standard scores, raw scores and/or score transformations) and will participate in the dissemination of findings from this project. He will also oversee study personnel including the project manager and PhD student.

## CO-INVESTIGATORS

### Jack Noble, PhD

[redacted] calendar months, Years 1-5

Dr. Noble is an assistant professor and engineer at Vanderbilt University who is chiefly responsible for the development, implementation, and revision of the **I**mage-**G**uided **C**ochlear **I**mplant **P**rogramming (IGCIP) model, database, and associated software. Dr. Noble will play a vital role in the execution of the proposed project in which he will guide our exploration of IGCIP for all enrolled participants.

### Benoit Dawant, PhD

[redacted] academic months, Years 1-5

Dr. Dawant is a Professor and an engineer who has had over two decades of experience in image-guided surgery and analysis. He is vital member of the IGCIP research team and has played an integral role in the development and refinement of the algorithms, associated database, and software implementation. Dr. Dawant's expertise and insight will be of critical value to the successful execution of IGCIP for the proposed patient population.

### Robert Labadie, MD, PhD

[redacted] calendar months Years 1-5

Dr. Labadie is both an otologic surgeon and an engineer with extensive experience in the development and implementation of our IGCIP research program. Because he is a surgeon who routinely implants pediatric patients, he intimately understands the research questions and will thus provide valuable insight into the execution of the experiments, recruitment of study participants, and data analysis—particularly with respect to specific aim 1.

### Mary Dietrich, PhD

[redacted] calendar months Years 1-4, [redacted] calendar months in Year 5

Dr. Dietrich is a biostatistician who has a history of collaborative research and publication with the PIs on behavioral research projects examining speech, language, and hearing outcomes.

## CONSULTANTS

### Susan Nittrouer, PhD

Dr. Nittrouer has been listed as a consultant as her input and experience with childhood language with our target study population (i.e. children with cochlear implants) will be of critical value to the project. [redacted] annually has been budgeted for consulting with Dr. Nittrouer. This includes up to 5 full days consulting per year plus travel expenses (airfare, lodging and meals, [redacted] per year)

### Ferenc Bunta, PhD

Dr. Bunta has been listed as a consultant as his expertise in speech production and accompanying acoustic analysis will be of great value to aim 2 of the proposed project. [redacted] annually has been budgeted for consulting with Dr. Bunta which includes bi-monthly videoconferences and 1 on-site visit per year during which he will provide guidance regarding acoustic analyses of the speech production wave files obtained for each study participant.

**PROGRAMMER, TBD**

A computer programmer with expertise in MATLAB® will be consulted on a PRN basis as shown here. Programming will be primarily used to refine the computer-controlled administration of the psychoacoustic measures. We anticipate that the majority of the programming will be needed in years 1 & 2:

Year 1: [redacted]
Year 2: [redacted]
Year 3-5: [redacted]

**SPEECH PRODUCTION ANALYSIS: AURAL ANALYTICS**

Aural analytics has a specific set of acoustic tools to serve as a proxy for measuring articulation changes in speech production that may not be measurable via human factors. The speech analysis software will provide measures of 1) vocal quality i.e., harmonic-to-noise ratio, 2) pitch (F0, mean, SD, range), 3) articulatory control, and 4) nasality. Data will be collected on an iPad equipped with Aural Analytics software (see equipment budget). The costs include a combined fee of automated and backup human coded/verified analyses for 60 study participants at baseline and two post-intervention visits. We have budgeted [redacted] for years 1-4 and [redacted] for year 5 to complete these analyses.

**OTHER PERSONNEL**

**Project Manager (TBD)**

[redacted] calendar months Years 1-5

Funding for 1.0 FTE project manager working on this project, is requested for all five years of the grant. The project manager will manage participant recruitment, the secure web-based database “REDCap” (Research Electronic Data Capture), data collection, data entry, and all matters pertaining to the IRB. In addition to the PIs, the project manager will also interact directly with the clinical team at the Vanderbilt Bill Wilkerson Center Audiology Clinic to ensure that pediatric CI patients are provided with information regarding the study. Because much of the research activities involve audiologic and speech/language measurement and practice, this individual will ideally be a certified and licensed audiologist or speech/language pathologist with research interest. The project manager will be trained by the PIs in responsible conduct of research and ethics of research and will complete the CITI training course on the Protection of Human Subjects. Finally, the project manager will assist out-of-town participants with travel management including air/ground transportation and hotel accommodations.

**Staff engineer (TBD)**

[redacted] calendar months Years 1-5

A staff engineer/database specialist will be required who maintains the current IGCIP database and associated web-based portals that permit uploading CT images, storing plans, setting calendars, and communication between study personnel. She will be responsible for maintaining the database and for the transfer of images and plans. She will also assist in the creation of plans and on the modification of the planning tools and the database necessary to support new IGCIP techniques.

**STUDENTS**

**GRA, 1 PhD student, TBD**

[redacted] calendar months Years 1-5

Funding for one PhD student is requested for all five years of the grant [redacted] FTE working [redacted] on this project). The PhD students will work up to 20 hours/week on the project and their compensation will not exceed limitations of NIH NRSA stipends. The student will assist with subject recruitment, data collection, data entry, and overall lab management with respect to the proposed research activities.

**Student Health Insurance:** Student health insurance is estimated at [redacted]/year.

**Tuition:** Tuition support is requested for the PhD graduate student for [redacted] of Vanderbilt's graduate tuition and student health insurance. *Tuition is excluded from the indirect cost calculations*.

Estimated annual tuition expense: [redacted]

**LAB SUPPLIES**

Year 1

| | |
|---|---|
| Leiter International Performance Scale, 3rd edition | [redacted] |
| Expressive One Word Picture Vocabulary Test | [redacted] |
| Receptive One Word Picture Vocabulary Test | [redacted] |
| Test of Auditory Comprehension of Language | [redacted] |
| Comprehensive Test of Phonological Processes | [redacted] |
| Woodcock-Johnson Tests of Achievement | [redacted] |
| Renfrew Bus Story—North American (RSB-NA) | [redacted] |
| PedsQL 4.0 | [redacted] |
| iPad with Aural Analytics software | [redacted] |
| General lab supplies | [redacted] |

General Lab Supplies

Year 2-5: [redacted]

**TRAVEL & CONFERENCE ATTENDANCE**

| | |
|---|---|
| YEAR 1: ASHA, 2 attendees | [redacted] |
| YEAR 2: ASHA, 2 attendees | [redacted] |
| YEAR 3: ASHA, 2 attendees; AAS, 1 attendee, Conference on Implantable Auditory Prostheses (CIAP) 1 attendee | [redacted] |
| YEAR 4: ASHA, 1 attendee; ACIA, 1 attendee, Hearing Across the Lifespan, 1 attendee | [redacted] |
| YEAR 5: ASHA, 2 attendees, SRCD, 1 attendee | [redacted] |

**STUDY PARTICIPANT FEES:**

**Participant Remuneration**

**Year 1:** [redacted]
**Year 2:** [redacted]
**Year 3:** [redacted]
**Year 4:** [redacted]
**Year 5:** [redacted]

We anticipate having to recruit a proportion of our pediatric CI recipients from outside the greater Nashville metropolitan area. We are budgeting for ground travel and hotel accommodations for approximately 40% of our study population (pediatric study participant and a parent). Our patient population includes much of the southeastern U.S. with many of our pediatric patients residing in west or east Tennessee—residences which can be over 300 miles from the Vanderbilt University Medical Center. Thus, we are budgeting for mileage reimbursement, plus 2 nights' hotel [redacted], and meals for [redacted] of our proposed study population over the 5-year period, as follows:

**Participant Travel**

**Year 1:** [redacted]
**Year 2:** [redacted]
**Year 3:** [redacted]
**Year 4:** [redacted]
**Year 5:** [redacted]

# RESEARCH & RELATED BUDGET - Cumulative Budget

| | Totals ($) |
|---|---|
| Section A, Senior/Key Person | [redacted] |
| Section B, Other Personnel | [redacted] |
| Total Number Other Personnel | 10 |
| Total Salary, Wages and Fringe Benefits (A+B) | [redacted] |
| Section C, Equipment | [redacted] |
| Section D, Travel | [redacted] |
| 1. Domestic | [redacted] |
| 2. Foreign | [redacted] |
| Section E, Participant/Trainee Support Costs | [redacted] |
| 1. Tuition/Fees/Health Insurance | [redacted] |
| 2. Stipends | [redacted] |
| 3. Travel | [redacted] |
| 4. Subsistence | [redacted] |
| 5. Other | [redacted] |
| 6. Number of Participants/Trainees | 0 |
| Section F, Other Direct Costs | [redacted] |
| 1. Materials and Supplies | [redacted] |
| 2. Publication Costs | [redacted] |
| 3. Consultant Services | [redacted] |
| 4. ADP/Computer Services | [redacted] |
| 5. Subawards/Consortium/Contractual Costs | [redacted] |
| 6. Equipment or Facility Rental/User Fees | [redacted] |
| 7. Alterations and Renovations | [redacted] |
| 8. Other 1 | [redacted] |
| 9. Other 2 | |
| 10. Other 3 | |
| Section G, Direct Costs (A thru F) | [redacted] |
| Section H, Indirect Costs | [redacted] |
| Section I, Total Direct and Indirect Costs (G + H) | [redacted] |
| Section J, Fee | [redacted] |
| Section K, Total Costs and Fee (I + J) | [redacted] |





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Enter name of Organization:** Vanderbilt University

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Jack | H | Noble | | PD/PI | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 2 . | | Benoit | | Dawant | | Co-Investigator | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 3 . | | Mary | S. | Dietrich | | Biostatistician | [redacted] | [redacted] | | | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | TBA Staff Engineer | [redacted] | | | [redacted] | [redacted] | [redacted] |
| **1** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

**C. Equipment Description**

List items and dollar amount for each item exceeding $5,000

| **Equipment Item** | **Funds Requested ($)*** |
|---|---|
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | |
| 2. Foreign Travel Costs | |
| **Total Travel Cost** | |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | |
| 2. Stipends | | |
| 3. Travel | | |
| 4. Subsistence | | |
| 5. Other: | | |
| **Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| Total Other Direct Costs | |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| Total Direct Costs (A thru F) | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC | [redacted] | [redacted] | [redacted] |
| | | Total Indirect Costs | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| Total Direct and Indirect Institutional Costs (G + H) | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: Budget Justification.pdf<br>(Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Enter name of Organization:** Vanderbilt University

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Jack | H | Noble | | PD/PI | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 2 . | | Benoit | | Dawant | | Co-Investigator | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 3 . | | Mary | S. | Dietrich | | Biostatistician | [redacted] | [redacted] | | | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | TBA Staff Engineer | [redacted] | | | [redacted] | [redacted] | [redacted] |
| **1** | **Total Number Other Personnel** | | | | **Total Other Personnel** | | [redacted] |
| | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

**C. Equipment Description**

List items and dollar amount for each item exceeding $5,000

| **Equipment Item** | **Funds Requested ($)*** |
|---|---|
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | |
| 2. Foreign Travel Costs | |
| **Total Travel Cost** | |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | |
| 2. Stipends | | |
| 3. Travel | | |
| 4. Subsistence | | |
| 5. Other: | | |
| **Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| Total Other Direct Costs | |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| Total Direct Costs (A thru F) | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC | 57.00 | [redacted] | [redacted] |
| | | Total Indirect Costs | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| Total Direct and Indirect Institutional Costs (G + H) | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: Budget Justification.pdf<br>(Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Enter name of Organization:** Vanderbilt University

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Jack | H | Noble | | PD/PI | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 2 . | | Benoit | | Dawant | | Co-Investigator | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 3 . | | Mary | S | Dietrich | | Biostatistician | [redacted] | [redacted] | | | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | TBA Staff Engineer | [redacted] | | | [redacted] | [redacted] | [redacted] |
| **1** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

**C. Equipment Description**

List items and dollar amount for each item exceeding $5,000

| **Equipment Item** | **Funds Requested ($)*** |
|---|---|
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | |
| 2. Foreign Travel Costs | |
| **Total Travel Cost** | |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | |
| 2. Stipends | | |
| 3. Travel | | |
| 4. Subsistence | | |
| 5. Other: | | |
| **Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| Total Other Direct Costs | |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| Total Direct Costs (A thru F) | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC | [redacted] | [redacted] | [redacted] |
| | | Total Indirect Costs | [redacted] |

| | |
|---|---|
| **Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number) | Department of Health and Human Services , Steven Zuraf (301) 492-4855 |

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| Total Direct and Indirect Institutional Costs (G + H) | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: Budget Justification.pdf (Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Enter name of Organization:** Vanderbilt University

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Jack | H | Noble | | PD/PI | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 2 . | | Benoit | | Dawant | | Co-Investigator | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 3 . | | Mary | S | Dietrich | | Biostatistician | [redacted] | [redacted] | | | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | TBA Staff Engineer | [redacted] | | | [redacted] | [redacted] | [redacted] |
| **1** | **Total Number Other Personnel** | | | | | **Total Other Personnel** | [redacted] |
| | | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

**C. Equipment Description**

List items and dollar amount for each item exceeding $5,000

| **Equipment Item** | **Funds Requested ($)*** |
|---|---|
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |

**Additional Equipment:** File Name:

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | |
| 2. Foreign Travel Costs | |
| **Total Travel Cost** | |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | |
| 2. Stipends | | |
| 3. Travel | | |
| 4. Subsistence | | |
| 5. Other: | | |
| **Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| Total Other Direct Costs | |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| Total Direct Costs (A thru F) | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC | [redacted] | [redacted] | [redacted] |
| | | Total Indirect Costs | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number) Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| Total Direct and Indirect Institutional Costs (G + H) | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

| L. Budget Justification* | File Name: Budget Justification.pdf<br>(Only attach one file.) |
|---|---|

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

# RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Enter name of Organization:** Vanderbilt University

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

**A. Senior/Key Person**

| | Prefix | First Name* | Middle Name | Last Name* | Suffix | Project Role* | Base Salary ($) | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits ($)* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 . | | Jack | H | Noble | | PD/PI | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 2 . | | Benoit | | Dawant | | Co-Investigator | [redacted] | | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |
| 3 . | | Mary | S | Dietrich | | Biostatistician | [redacted] | [redacted] | | | [redacted] | [redacted] | [redacted] |

**Total Funds Requested for all Senior Key Persons in the attached file**

**Additional Senior Key Persons:** File Name:

**Total Senior/Key Person** [redacted]

**B. Other Personnel**

| Number of Personnel* | Project Role* | Calendar Months | Academic Months | Summer Months | Requested Salary ($)* | Fringe Benefits* | Funds Requested ($)* |
|---|---|---|---|---|---|---|---|
| | Post Doctoral Associates | | | | | | |
| | Graduate Students | | | | | | |
| | Undergraduate Students | | | | | | |
| | Secretarial/Clerical | | | | | | |
| 1 | TBA Staff Engineer | [redacted] | | | [redacted] | [redacted] | [redacted] |
| **1** | **Total Number Other Personnel** | | | | **Total Other Personnel** | | [redacted] |
| | | | | | **Total Salary, Wages and Fringe Benefits (A+B)** | | [redacted] |

RESEARCH & RELATED Budget {A-B} (Funds Requested)





Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ❍ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

| **C. Equipment Description** | |
|---|---|
| List items and dollar amount for each item exceeding $5,000 | |
| **Equipment Item** | **Funds Requested ($)*** |
| **Total funds requested for all equipment listed in the attached file** | |
| **Total Equipment** | |
| **Additional Equipment:** File Name: | |

| **D. Travel** | **Funds Requested ($)*** |
|---|---|
| 1. Domestic Travel Costs ( Incl. Canada, Mexico, and U.S. Possessions) | |
| 2. Foreign Travel Costs | |
| **Total Travel Cost** | |

| **E. Participant/Trainee Support Costs** | | **Funds Requested ($)*** |
|---|---|---|
| 1. Tuition/Fees/Health Insurance | | |
| 2. Stipends | | |
| 3. Travel | | |
| 4. Subsistence | | |
| 5. Other: | | |
| **Number of Participants/Trainees** | **Total Participant Trainee Support Costs** | |

RESEARCH & RELATED Budget {C-E} (Funds Requested)



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

**ORGANIZATIONAL DUNS*:** [redacted]

**Budget Type*:** ○ Project ● Subaward/Consortium

**Organization:** Vanderbilt University

**Start Date*:** 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

| F. Other Direct Costs | Funds Requested ($)* |
|---|---|
| Total Other Direct Costs | |

| G. Direct Costs | Funds Requested ($)* |
|---|---|
| Total Direct Costs (A thru F) | [redacted] |

**H. Indirect Costs**

| Indirect Cost Type | Indirect Cost Rate (%) | Indirect Cost Base ($) | Funds Requested ($)* |
|---|---|---|---|
| 1 . MTDC | [redacted] | [redacted] | [redacted] |
| | | Total Indirect Costs | [redacted] |

**Cognizant Federal Agency** (Agency Name, POC Name, and POC Phone Number): Department of Health and Human Services , [redacted]

| I. Total Direct and Indirect Costs | Funds Requested ($)* |
|---|---|
| Total Direct and Indirect Institutional Costs (G + H) | [redacted] |

| J. Fee | Funds Requested ($)* |
|---|---|
| | |

| K. Total Costs and Fee | Funds Requested ($)* |
|---|---|
| | [redacted] |

**L. Budget Justification*** File Name: Budget Justification.pdf

(Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

**Vanderbilt Budget Justification**

**PERSONNEL**

**Jack Noble, PhD**
[redacted] academic months and [redacted] summer months, Years 1-5
Dr. Noble is an assistant professor and engineer at Vanderbilt University who is chiefly responsible for the development, implementation, and revision of the **I**mage-**G**uided **C**ochlear **I**mplant **P**rogramming (IGCIP) model, database, and associated software. He will serve as site PI at Vanderbilt University and will play a vital role in the execution of the proposed project. He will oversee software modifications and the creation of IGCIP plans for the 60 cochlear implant recipients in this study.

**Benoit Dawant, PhD**
[redacted] academic months and [redacted] summer months, Years 1-5
Dr. Dawant is a Professor and an engineer who has had over two decades of experience in image-guided surgery and analysis. He is vital member of the IGCIP research team and has played an integral role in the development and refinement of the algorithms, associated database, and software implementation. Dr. Dawant will oversee modifications to the IGCIP database for this project. His expertise and insight will be of critical value to the successful execution of IGCIP for the proposed patient population.

**Mary Dietrich, PhD**
[redacted] calendar months, Years 1-4, [redacted] calendar months, Years 5
Dr. Dietrich is a biostatistician who has a history of collaborative research and publications with the PIs on behavioral research projects examining speech, language, and hearing outcomes. She will be providing statistical consult and guidance in years 4 and 5.

**Staff Engineer, TBD**
[redacted] calendar months Years 1-5
A staff engineer/database specialist will be identified to modify the existing IGCIP database and associated web-based portals for use in this project. These systems permit uploading images, storing plans, setting calendars, and communication between study personnel. The engineer will be responsible for maintaining the database and for the transfer of images and plans. The engineer will also assist in the creation of plans and on any modification of the planning software necessary to support this project.

# RESEARCH & RELATED BUDGET - Cumulative Budget

| | Totals ($) |
|---|---|
| Section A, Senior/Key Person | [redacted] |
| Section B, Other Personnel | [redacted] |
| Total Number Other Personnel | 5 |
| Total Salary, Wages and Fringe Benefits (A+B) | [redacted] |
| Section C, Equipment | |
| Section D, Travel | |
| 1. Domestic | |
| 2. Foreign | |
| Section E, Participant/Trainee Support Costs | |
| 1. Tuition/Fees/Health Insurance | |
| 2. Stipends | |
| 3. Travel | |
| 4. Subsistence | |
| 5. Other | |
| 6. Number of Participants/Trainees | |
| Section F, Other Direct Costs | |
| 1. Materials and Supplies | |
| 2. Publication Costs | |
| 3. Consultant Services | |
| 4. ADP/Computer Services | |
| 5. Subawards/Consortium/Contractual Costs | |
| 6. Equipment or Facility Rental/User Fees | |
| 7. Alterations and Renovations | |
| 8. Other 1 | |
| 9. Other 2 | |
| 10. Other 3 | |
| Section G, Direct Costs (A thru F) | [redacted] |
| Section H, Indirect Costs | [redacted] |
| Section I, Total Direct and Indirect Costs (G + H) | [redacted] |
| Section J, Fee | |
| Section K, Total Costs and Fee (I + J) | [redacted] |

**Total Direct Costs less Consortium F&A**

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

| Category | Budget Period 1 | Budget Period 2 | Budget Period 3 | Budget Period 4 | Budget Period 5 | TOTALS |
|---|---|---|---|---|---|---|
| Total Direct Costs less Consortium F&A | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] | [redacted] |

# PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

## 1. Vertebrate Animals Section

Are vertebrate animals euthanized? ○ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

○ Yes ○ No

If "No" to AVMA guidelines, describe method and provide scientific justification

## 2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

| *Budget Period | *Anticipated Amount ($) | *Source(s) |
|---|---|---|



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# PHS 398 Cover Page Supplement

## 3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ❍ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

## 4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ❍ Yes ❍ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ❍ Yes ❍ No

## 5. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:



Tracking Number: GRANT12696653 Funding Opportunity Number: PA-18-334 . Received Date: 2018-08-16T11:14:30.000-04:00

# PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 03/31/2020

| | |
|---|---|
| **Introduction** | |
| 1. Introduction to Application (for Resubmission and Revision applications) | M-18_PHS_ResearchPlan_IntroductionToApplication.pdf |
| **Research Plan Section** | |
| 2. Specific Aims | M-6_PHS_ResearchPlan_SpecificAims.pdf |
| 3. Research Strategy* | M-11_PHS_ResearchPlan_ResearchStrategy.pdf |
| 4. Progress Report Publication List | |
| **Other Research Plan Section** | |
| 5. Vertebrate Animals | |
| 6. Select Agent Research | |
| 7. Multiple PD/PI Leadership Plan | M-10_PHS_ResearchPlan_MultiplePILeadershipPlan.pdf |
| 8. Consortium/Contractual Arrangements | M-7_PHS_ResearchPlan_ConsortiumContractualArrangements.pdf |
| 9. Letters of Support | M-8_PHS_ResearchPlan_LettersOfSupport.pdf |
| 10. Resource Sharing Plan(s) | M-9_PHS_ResearchPlan_ResourceSharingPlans.pdf |
| 11. Authentication of Key Biological and/or Chemical Resources | |
| **Appendix** | |
| 12. Appendix | |



Tracking Number: GRANT12696653
Funding Opportunity Number: PA-18-334. Received Date: 2018-08-16T11:14:30.000-04:00

**INTRODUCTION**

This is a resubmission of 1 R01 DC017683-01 entitled *Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy*. The reviewers invested considerable time in the review of this application and their efforts to provide a thorough and objective review are genuinely appreciated. We have endeavored to address all critiques. As a result, we are confident that the reviewers' valuable advice has greatly enhanced the quality of this application. In accord with NIH's newest guidelines for A1 applications, we have not highlighted changes in the research strategy; however, all changes are summarized below.

**General comments**: There was consensus among reviewers on the following weaknesses: **1)** blinding, **2)** timeline, **3)** working memory, **4)** ceiling effects, **5)** greater detail regarding age range and analysis plan, and **6)** reliability of standardized measures. Detail is provided below for each point.

**1) Blinding:** This is an excellent suggestion and adds scientific rigor. The revised experimental plan now includes blinding of both experimenters and participants. Only the PIs and Co-I, Dr. Dietrich—who will generate the randomization scheme—will know whether the participant is in the immediate intervention or deferred waitlist group until the end of the study. Neither PI or Dr. Dietrich will be administering assessments nor scoring test for any of the participants. Additional blinding detail, including provisions for breaking the blind, are located in the application in *Approach*, *Data Safety and Monitoring Plan,* and *Statistical Design and Power Analyses*.

**2) Timeline:** We have added much greater detail to the timeline in accord with clinical trial guidelines.

**3) Working memory:** We recognize that working memory could confound the results and thus we have added working memory controls to the study. We will administer 3 assessments of working memory including the Numbers Reversed test from the 4$^{th}$ edition of the Woodcock Johnson Test of Cognitive Ability and two tasks developed by project consultant Dr. Nittrouer including a serial recall task and visual-spatial task. We will be using the "W" score from the WJ-4 Numbers Reversed test, which is a weighted raw score that, unlike standard scores, permits direct comparisons of ability levels across age ranges. The serial recall and visual-spatial tasks yield criterion scores than can be standardized across participants. We will statistically control for working memory by partialling out individual pre-intervention working memory levels from the pre- to post-intervention gain scores on the treatment outcome measures of interest (e.g., phonological awareness, language). Greater detail for all 3 tasks is included in the *Approach*.

**4) Ceiling effects:** Ceiling effects—defined here as a baseline score > 80% correct—were an issue for many participants on measures of speech recognition in quiet. For speech recognition in noise as shown in Figure 5, only 30% of the subjects exhibited ceiling level performance for +5 dB signal-to-noise ratio (SNR). However, we do recognize that this could prove problematic in this randomized clinical trial (RCT) with a larger population. Thus, we have added an adaptive speech receptive threshold in semi-diffuse background noise providing a threshold, in dB SNR, required for 50% correct performance. We have administered this task to pediatric and adult CI recipients and have published normative data for children and adults (1,2). We have also added the quasi-adaptive BKB-SIN measure which also provides a score, in dB SNR, for 50% correct; further, the BKB-SIN is recommended for use in this population by the pediatric minimum speech test battery (PMSTB) working group (3) thereby strengthening clinical relevance of the auditory assessment battery. Due to the adaptive nature of the speech receptive threshold and BKB-SIN measures, ceiling effects are not encountered for individuals with hearing loss. Because we had originally included the BKB-SIN in our preliminary studies, we have baseline and post-intervention data for 19 participants [18 of whom are included in Noble et al. (4)]. Baseline and post-IGCIP data for the BKB-SIN test are now described in the application in *Preliminary Studies*.

**5) Details re: age range and analysis plan:** We acknowledge that we did not provide sufficient detail regarding the age range of participants included in our preliminary studies. We have now included the age range for the 41 participants' data included in the *Preliminary Studies* section as 4.4 to 17.9 years (mean = 9.8). The age range we will include in the proposed studies will be 6 to 12 years; thus 32 of the 41 participants (78%) were in the age range specified in the application and all in this age range were able to complete the auditory test battery as proposed. This provided us with feasibility data motivating the chosen age range as all should be capable of completing a comprehensive behavioral battery of auditory perception. All measures of speech, language, phonological awareness, working memory, and literacy are routinely completed in this age range and have age normative data. With respect to the analysis plan, we have provided greater detail regarding our plans for analysis of longitudinal data and how measures of working memory will be factored as a covariate. Biostatistician and Co-I, Dr. Dietrich, has edited and clarified this section of the proposal.

**6) Reliability of standardized measures:** We have examined the test-retest reliability for all standard measures in the battery for the age range we plan to include. Because 6- to 12-year olds are relatively consistent responders to the testing procedures herein, the reliability coefficients are all above 0.90 according to the test manuals. We have added this information to the approach.

**SPECIFIC AIMS**

Although children with cochlear implants (CIs) have significantly improved speech, language, and reading outcomes relative to previous generation CI recipients, too many pediatric CI users still display persistent speech, language, and reading difficulties despite early implantation and early intervention [see (5–7)]. Children with CIs typically lag behind their peers with normal hearing (NH) by 1 or more years on measures of speech, language and/or reading [e.g., (8–15)]. Though these persistent delays can be attributed in part to a period of auditory deprivation prior to implantation (12,16,17), increasing evidence suggests that a degraded CI signal is also implicated in poorer development of auditory, speech, language, and reading skills for pediatric CI recipients (6,18–22). A related developmental path to reading also disrupted from the degraded CI signal is phonological awareness (PA) because PA is predicated, in part, on speech recognition (23).

A procedure developed by Noble and colleagues (4,24–26), ***image-guided CI programming (IGCIP),*** significantly improves auditory function, speech recognition, and distally, receptive language abilities for adult CI users. We have preliminary evidence that pediatric CI recipients also significantly benefit from ***IGCIP*** (4). But there is a need to systematically investigate IGCIP in children to determine whether this individualized intervention yields a) associated benefits in auditory function and b) related improvements in speech, language, PA and/or reading. ***Thus, our primary goal is to evaluate the effects of IGCIP on auditory function, speech recognition, PA and reading, as well as speech and language abilities in pediatric CI recipients within the context of a double blind, waitlist controlled randomized clinical trial (RCT).*** We will obtain psychophysical estimates of auditory function and speech recognition, PA, reading, speech, and language abilities for 60 pediatric CI users in a baseline assessment and repeated time points for 24 months to test the impact of IGCIP. We will examine the immediate (short-term) and longer-term effects over a 2-year period by comparing outcomes between groups for those randomly assigned to immediate (n = 30) or deferred (n = 30) IGCIP using a *waitlist control study design (deferred IGCIP)*. The initial comparison will be for immediate and deferred IGCIP groups at 2, 6, and 12 months. The deferred group will then receive the IGCIP intervention and both groups will be followed for an additional 12 months (total enrollment for 24 months). The proposed research includes the following aims and specific hypotheses:

**Aim 1: Auditory function.** We will compare auditory function and speech recognition of the immediate and waitlist control participants**.** Hypothesis 1a: There will be significant positive short-term gains (2-6 months) in spectral and/or temporal resolution as well as speech recognition—particularly in noise—for children immediately receiving IGCIP as compared to waitlist controls. This hypothesis will be tested by comparing the difference in the amount of change in scores within-subjects (pre- to post-IGCIP gain) between the groups (treated vs. untreated) controlling for initial scores. Hypothesis 1b: IGCIP gain in spectral and/or temporal resolution will significantly predict gain in speech recognition. This hypothesis will be tested via regression analyses of change in speech recognition scores on change in resolution, controlling for baseline values and also controlling for baseline levels of speech recognition and working memory.

**Aim 2: PA and reading.** We will explore the complex relationships amongst auditory function, speech recognition, PA, and reading ability. Hypothesis 2a: **Differential *growth*** in spectral/temporal resolution and/or speech recognition will predict growth in PA, which in turn will predict mediated growth in reading. Hypothesis 2b: Growth in PA will be associated with amount of IGCIP benefit (gain) and will mediate growth in reading, which will be tested via cross-legged panel and path analyses. Note that testing these hypotheses is not dependent on the outcomes of Aim 1 as *only variable gain in the Aim 1 measures (e.g., speech recognition) are required for aim 2 analyses,* not a significant between-group difference for IGCIP in Aim 1.

**Aim 3: Speech and language.** We will compare pre- and post-IGCIP receptive and expressive language abilities and speech production of pediatric CI recipients to the waitlist control group. We will test these skills at various time points on standardized and clinical measures of 1) receptive language, 2) expressive language, and 3) speech production (articulation and acoustic analyses)*.* Hypothesis 3a: There will be significant differences between groups for positive growth in speech and language and this growth will be *predicted* by the relative improvement in auditory function (aim 1) from IGCIP while controlling for baseline levels of working memory. Hypothesis 3b: Spectral/temporal resolution and speech recognition and/or PA will serve as *mediators* of expressive and receptive language gains and speech production gains both within and between groups. 3a and 3b will also be tested using mixed effects modeling and regression analyses to examine these “downstream” effects. *Even if no between group differences in Aim 1 and/or Aim 2 are seen, we will nonetheless be able to test whether spectral/temporal resolution, speech recognition, and/or PA predict growth in receptive and/or expressive language and/or changes in speech production (including subclinical acoustic analyses).*

## RESEARCH STRATEGY

### SIGNIFICANCE

Cochlear implant (CI) technology yields significant improvement in auditory function, speech recognition, speech production, language, reading, and overall quality of life for the majority of recipients. Despite such advances, pediatric CI recipients continue to display significant variability in speech and language development with too many recipients continuing to display poor outcomes [e.g., (10,14,15,17,27–31)]. A recent study of pediatric CI users brought these issues into sharp focus: Dettman et al. (2016) investigated speech recognition and language outcomes for a large cohort of pediatric CI recipients (n = 403) who were all educated in an inclusion classroom using listening and spoken language as the primary mode of communication (17). **Figure 1** is a reproduction of data illustrating mean standard scores for language and vocabulary for all children upon entry into 1st grade (14). This figure displays the magnitude and pervasive nature of the deficits across language measures for even the group of children implanted under 24 months (green bars). Indeed, all means were at least 1 standard deviation below the age normative range.

Clearly, there is an ongoing need to improve language outcomes in these children (7). The source of delay is partially attributed to a period of auditory deprivation prior to implantation [e.g., (12,16)]. However, it is also likely that an impoverished CI signal is implicated in ongoing poorer-than-normal development on measures of auditory, speech, language, and reading (8,22,32). Several researchers have documented extremely poor spectral resolution for pediatric CI users—much poorer than that exhibited by adult CI recipients (20,33–37). Such findings suggest that pediatric CI users with prelingual deafness may not depend upon spectral resolution for speech recognition in the same manner as adults, particularly in noisy environments. Indeed Lowenstein & Nittrouer (19) recently demonstrated that children with hearing loss—using hearing aids and CIs—placed ***significantly less weight on spectral cues*** than children with NH. In contrast, the children with CIs placed ***greater weight on amplitude cues***—related to temporal envelope perception—as compared to the children with NH (19). Thus, it is possible that young children with CIs are making use of *different cues*, such as those contained within the temporal envelope, or spectrotemporal contrasts, both of which have been shown to yield high levels of consonant recognition in NH adults (e.g., (38–41)]. Further investigation is warranted to investigate the relationship between spectral resolution, temporal resolution, and speech recognition so that we can identify the underlying mechanisms driving speech recognition in pediatric CI users as well as links to PA, reading, speech, and language abilities. Understanding the underlying mechanisms driving speech recognition in pediatric CI users is not only necessary for theoretical purposes, but this information is critical to maximize a child's auditory abilities in the context of both CI programming and, ultimately, for speech/language/reading intervention. For example, if we learn that children are using different auditory cues to drive speech recognition—such as greater weight on temporal vs. spectral cues—we could select CI stimulation parameters that best transmit a *well-defined temporal envelope* such as high channel stimulation rates [>1500 pulses per second (42–44)] and removal of current steering which can introduce fluctuations in the temporal envelope that are uncorrelated with the incoming signal (45). In contrast, should we find that children rely heavily on spectral resolution and/or spectrotemporal cues as adult CI recipients do, we could choose image-guided programming strategies designed to transmit finer spectral detail—such as patient-specific electrode deactivation to improve spatial selectivity of intracochlear excitation patterns and its psychological correlate, spectral resolution.

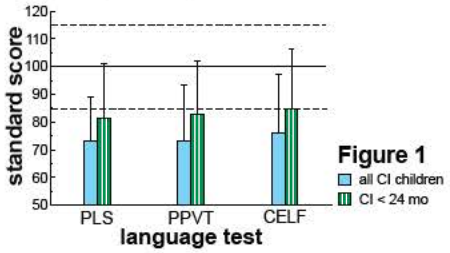



**Figure 1**

**Image-guided CI programming (IGCIP)**

Our team has pioneered the use of postoperative CT scanning of CI users to delineate the CI electrode-neural interface and use this information to create customized programming maps. We refer to this process as image-guided cochlear implant programming (IGCIP) and here describe how it is performed. We have constructed an atlas based on 10 µCT scans of human cadaveric cochleae in which scala tympani (ST), scala vestibuli (SV), and the modiolus have been manually delineated as these anatomical structures are not visually identifiable on clinical CT scans. Next, on a pre-operative clinical CT scan, this atlas is iteratively fit to the patient's own anatomy to minimize the sum of the squared distance between the bony outline of the cochlea, which is identifiable both on the clinical CT scan as well as via µCT. Next, a post-operative CT scan is obtained, the centerline of the electrode array extracted, and a 3D model of the electrode array fit to the scan. Finally, the pre- and post-op scans are superimposed upon each other as the bony anatomy is consistent. The

output (top panel, **Figure 2**) includes 3D surfaces showing the position of individual electrodes relative to the neural endings they are intended to stimulate in the modiolus.

Next, we define the electrode-to-neural interface by calculating the distance-versus-frequency curves from the frequency mapped neural endings within the modiolus to each individual electrode. This is shown in the bottom panel of **Figure 2** where each of the colored curves represents a different electrode and shows the Euclidian distance from the electrode to the modiolus (ordinate) as well as the predicted frequency range of the modiolus (8) at that location (top abscissa). Electrodes are chosen for deactivation to minimize channel interaction—or spread of intracochlear electrical excitation. The premise is that such electrodes would be providing "redundant" electrical stimulation for a given segment of the cochlea. So, by deactivating these electrodes, we theorize that we are able to reduce channel interaction which should increase spatial selectivity of intracochlear electrical excitation. The heuristic we use to achieve this is to deactivate as few electrodes as possible while producing an overall curve with clearly defined local minima and with electrodes centered on the range of frequencies to which they are closest. Following this strategy for the example shown in **Figure 2**, we have deactivated electrodes 2, 3, 4, 6, 8, 10, and 16.

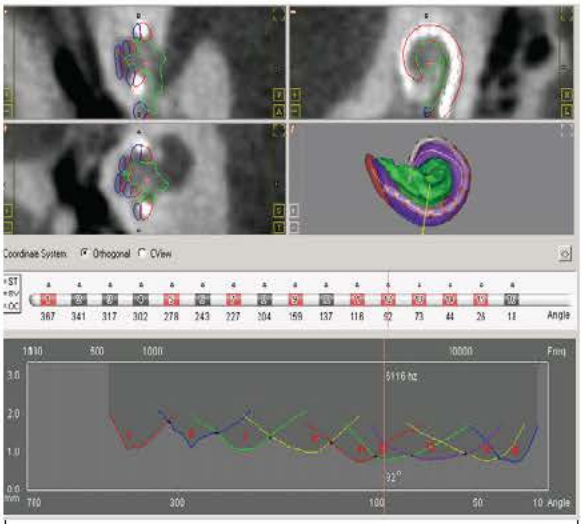



**Figure 2**: Software modu e def n ng e ectrode to neura nterface n CT scans and 3D reconstruct on (top pane : red=ST, b ue=SV, and green=mod o us). M dd e pane shows act ve e ectrodes n red. Bottom pane shows d stance vs frequency curves used to deact vate e ectrodes nterfer ng w th ne ghbor ng e ectrodes.

**Clinical significance: CI programming**

Clinical CI programming includes the mapping of incoming sound using a "one size fits all" approach of current limiting, frequency allocation, and stimulation of all electrodes. For some individuals, it is likely that these default programming methods provide a reasonable approximation to the patient's individualized anatomy and electrode location and that activation of all electrodes yields adequate outcomes. For other patients—particularly those who may exhibit poorer-than-average performance, have atypical cochlear anatomy, electrode dislocation, or extracochlear electrodes—a "one size fits all" approach will not afford the restoration of hearing that could be achieved had the recipient's anatomy and intracochlear electrode positioning been considered. For example, a recent study of 262 CI users showed that 13.4% of patients had at least 1 extracochlear electrode despite surgical reports of complete insertion (46). Active extracochlear electrodes will produce suboptimal high-frequency transmission as the acoustic information being transmitted to the *extracochlear electrodes* will not reach primary auditory neurons. Thus an additional goal of IGCIP is identification of extracochlear electrodes—critical information needed to ensure stimulus delivery of high frequency speech sounds (**Figure 6** preliminary studies). Such considerations are particularly critical for pediatric CI users for whom audibility of high-frequency stimuli is central to the acquisition of auditory-based speech and language.

Children are routinely implanted at ~12 months of age—the minimum age referenced by FDA labeled indications. Thus, it is the case that for the first 3 to 5 years of CI use, we are relying on external factors for CI programming and verification of CI map appropriateness. Such factors include "aided" audiometric thresholds, auditory skill development gauged primarily via parental questionnaire, and progress on measures of language and speech production. Even if a child is making progress, it is possible that using an individualized approach to CI parameter manipulation—capitalizing on the underlying hearing mechanisms driving performance as well as individualized anatomy and electrode location—would result in greater performance at a faster rate allowing for higher overall outcomes. Indeed, we have documented that pediatric CI recipients can derive significant benefit from IGCIP on measures of speech recognition in quiet and noise (4).

**Underlying mechanisms driving auditory-based speech recognition**

For adults with NH, speech recognition is dependent upon a high degree of spectral resolution of the individual components of speech including resolution of individual and relative formant frequencies as well as rapid formant transitions. Speech recognition—as dependent upon spectral resolution—poses a major obstacle for CI recipients and attempts to improve *spatial selectivity* of intracochlear electrical stimulation (i.e. reduction in channel interaction) have resulted in minimal improvements in speech recognition abilities [e.g., (47–50)]. Most attempts at improving intracochlear spatial selectively of electrical excitation patterns and subsequent improvements in spectral resolution, however, have investigated current focusing such as tripolar electrode

configuration [e.g., (51–58)] for adult CI users. Attempts at limiting channel interaction via current focusing have resulted in programming parameters and electrode configurations that significantly limit the dynamic range of electrical stimulation as well as significantly increase power demands for the sound processor. Such consequences render the applicability of these strategies clinically prohibitive.

Spectral resolution for CI users is often characterized using tasks of spectral modulation detection (SMD) or spectral ripple discrimination (e.g., (59–62)]. Numerous studies have shown a significant correlation between spectral resolution with a CI and auditory speech recognition *for adult CI users* (e.g., (60,63–69)]. Furthermore, researchers (45,70) have demonstrated that psychophysical measures of spectral resolution are more sensitive to changes in CI processing strategies and central auditory reorganization following implantation than traditional clinical measures of speech recognition (62,70). Thus it is common for researchers to use SMD as a proxy for channel interaction to determine whether CI programming changes may impact this phenomenon. Indeed we have shown that IGCIP yields statistically significant improvements in spectral resolution, via SMD, *in adult CI users* (24,26,49,71). In contrast to these findings, pediatric CI users exhibit extremely poor spectral resolution and estimates of pediatric CI spectral resolution are not significantly correlated with speech recognition [e.g., (20,37,72,73)] or were modestly correlated with vowel recognition in quiet (74). Furthermore there are conflicting reports regarding the relationship between listener age, age at CI, and overall spectral resolution abilities (20,72,74).

Description of underlying auditory mechanisms responsible for pediatric CI speech recognition is not only important for research purposes, but *holds significant clinical relevance*. To maximize outcomes for auditory function and related outcomes for speech, language, and literacy of our pediatric CI recipients, we must identify the auditory mechanisms driving speech recognition, whether those be spectral, temporal, or some combination thereof. The reason is that clinicians have access to a variety of CI signal coding strategies all focusing on different aspects of the incoming stimulus. For example, there are current-steering strategies designed to provide greater spectral representation of incoming stimuli (e.g., Fidelity-120, Optima), strategies designed to provide temporal fine structure in the apical channels via variable rate stimulation [e.g., fine structure processing], and high-rate strategies specifically designed to provide fine detail for temporal envelope representation at each stimulated electrode [e.g., HiRes, high-definition continuous interleaved sampling, and high-rate Advanced Combination Encoder]. Despite the known fact that adult and pediatric CI users demonstrate a significantly different relationship between spectral resolution and speech recognition (20,72,73), clinical audiologists are using the same default programming strategies (i.e. current steering and/or low-to-mid rate stimulation) with both adult and pediatric CI users within a one-size-fits-all philosophy. If we determine that pediatric CI users are more reliant on temporal coding for speech recognition, we can adapt a clinical approach to provide greater representation of temporal envelope with higher channel stimulation rates and removal of current steering. Ideally we would develop a data driven, personalized plan for CI programming capitalizing on the mechanisms driving auditory-based speech recognition combined with selective IGCIP channel activation to improve intracochlear spatial selectivity and resultant spectrotemporal resolution. Based on our published and preliminary data (4,20), our **hypotheses** are that IGCIP will improve 1) auditory function (spectral and/or temporal resolution), 2) speech recognition, and 3) improvements noted for spectral and temporal resolution will mediate improvements on measures of PA, speech production, language, and reading while controlling for confounds [e.g., nonverbal cognition, working memory (75–81)].

**Auditory Function, Speech Recognition, PA, and Reading**

Researchers and clinicians have been interested in the interrelationship between hearing, speech recognition, speech and language skills, PA, and reading outcomes for more than half a century (82–84). Until recently, speech recognition, speech production, language, PA and reading for children with CIs have been relatively poor and all domains have significantly lagged behind typically developing peers (6,8,21,30,85–88). Advances in CI technology have yielded dramatic improvements in all these domains. Indeed, recent reports have indicated that a number of CI recipients are trending into the typical range and in some cases, even into an advanced range for language and reading outcomes [e.g., (10,14,15,17,21,89)]. Despite these encouraging findings, a significant number of CI users continue to demonstrate relatively poor outcomes for speech, language, PA and/or reading. A likely explanation is that spectral resolution is strongly correlated with PA (90–92). Given the generally poor, but variable, spectral resolution abilities exhibited by pediatric CI recipients (20,72–74), it is not surprising that both PA and reading skills are often poorer than typically developing children. Despite the fact that pediatric CI users have poor spectral resolution and below average PA, some CI recipients are able to approach typical levels of performance on speech, language and reading achievement. ***One must then ask how are some children with CIs capable of achieving such high levels of speech***

***recognition and ultimately high levels of language and reading despite poor spectral and phonological processing?*** In other words, how are children with relatively poor spectral resolution able to bootstrap phonological decoding and subsequent reading? One explanation is grounded in **lexical restructuring theory** (93–96). Lexical restructuring theory posits that a child initially has a global representation of lexical information, and thus does not require fine spectral detail. As a child ages, she begins to learn phonotactic structure within her native language(s) and ultimately builds a more comprehensive lexicon (97). Nittrouer and colleagues reported that "Oral language skills explained more variance in emergent reading for children with CIs than for children with NH" suggesting that children who successfully build lexical and phonotactic representations despite incomplete spectral resolution will bootstrap PA and ultimately achieve higher vocabulary and reading levels (98,99). That is, converging syllable and lexical cues can be utilized to build partial phonotactic representations that are supported by non-spectral cues (i.e., temporal or spectrotemporal) (100). On the other hand, it is also plausible that some children cannot bootstrap the relative weaknesses in spectral resolution to PA (101) and thus continue to display poor vocabulary and reading skills. We hypothesize that improving intracochlear spatial selectivity via IGCIP will lead to improvements in auditory function and speech recognition, which will facilitate bootstrapping of PA. IGCIP could provide a direct unique path to benefit PA—a plausible hypothesis that can be tested in this experimental design.

There is a reliable relationship between speech recognition in noise and spectral resolution [e.g., (20,73,102,103)] and emerging data supporting a relationship between PA and spectral resolution (19). However, in the presence of poor spectral resolution for children with CIs, we must examine the relative contributions of alternative paths taken from speech recognition to PA, speech, language, and reading. **Figure 3** displays theorized models of IGCIP-mediated benefits of speech recognition and the subsequent effects on PA and receptive language. For example, it is plausible that there is an indirect path to PA mediated by a direct path through IGCIP-improved speech recognition. This can also be statistically tested within the context of a longitudinal double-blind, waitlist controlled RCT design, especially with measurements of potential mediators. A similar direct and indirect path can also be tested for IGCIP-gain scores in speech recognition and receptive language. Again, it is possible that IGCIP benefit directly improves receptive language and that this relationship is mediated via improvement in speech recognition resulting from IGCIP gain.

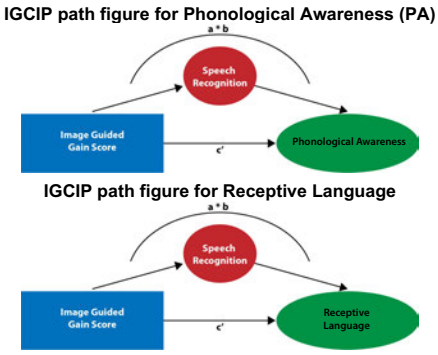



**Figure 3.** Direct and indirect (mediated) effects for GC P & speech recognition on PA and receptive language

Within the context of the current proposal, we have a unique opportunity to gain a better understanding of factors that predict speech, language, and reading outcomes in pediatric CI recipients. Specifically, the research activities proposed here can compare the growth in spectral and temporal resolution, speech recognition, PA, speech, language, and reading following IGCIP within the context of a double blind, waitlist controlled RCT. That is, hypothesized distal "benefits" resulting from refinement of intracochlear spatial selectivity via IGCIP can be systematically studied with a waitlist control longitudinal RCT. **Figure 3** includes examples of the basic design approach. A putative predictor, namely IGCIP gain scores for auditory function, can be tested as a direct and indirect predictor of speech recognition and PA. The direct path is from IGCIP gain to the outcome which may be PA and/or receptive language. The strength of the longitudinal RCT design is that the indirect path wherein speech recognition as a mediator of the relationship can also be tested. This design approach will also be employed to examine the direct and indirect relationships amongst speech recognition to receptive language, receptive language to expressive language, and receptive language to reading comprehension in addition to speech recognition to PA and PA to reading comprehension.

**IMPACT**

The impact of a **personalized approach to CI programming** on auditory function, speech recognition, PA, language, speech, and reading will be examined as a step in programmatic research designed to optimize auditory, speech, language, PA and reading outcomes in children with CIs. *Having access to personalized data regarding individualized anatomy, electrode location, and electrode-to-modiolus distances will make this investigation the first of its kind in the space of outcomes-based research for pediatric CI recipients.* The use of a randomized wait-list control design will not only afford a prospective and longitudinal investigation into the effects of IGCIP, but *this design will enable us to describe the expected growth trajectory for validated measures of speech recognition and psychophysical measures auditory perception for children with CIs over the course of a 2-year period*. Such data have never before been described with these measures and thus this

project offers high clinical relevance for audiologic management, test interpretation, and subsequent recommendations for pediatric CI recipients and their families.

## INNOVATION

This proposal is innovative in a number of ways. Although subsets of all of the potential relationships illustrated in **Figures 3 and 4** have been included piecemeal in cross-sectional and longitudinal studies of children with CIs, *previous studies have not included these measures in an integrated correlational longitudinal design nor have they considered individualized anatomical variations, electrode location, nor electrode-to-modiolus distances, while attempting to define the* ***mechanistic underpinnings of speech recognition in this population within the context of a double blind, waitlist controlled RCT.*** However, we have the benefit of these previous studies to power our analyses. We are also able to implement a newly developed refinement in CI programming to produce baseline changes in auditory function using IGCIP and then use this variability to refine the predictor models. In addition, the proposed research includes an innovative application of mediated analyses to test direct and indirect paths to the outcomes (i.e. PA and reading abilities) while controlling for confounds, including nonverbal intellectual skills and working memory. Our proposal challenges current clinical practices built on a "one size fits all" approach assuming that all CI users depend predominantly on spectral cues for auditory, speech, and language skills.

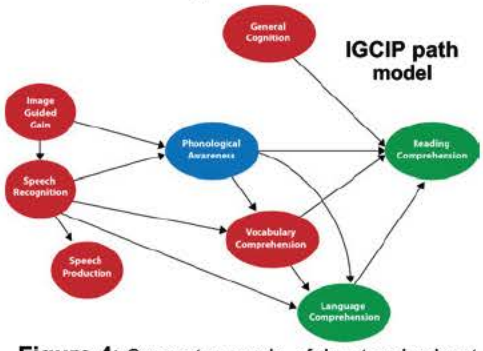



**Figure 4**: Conceptua mode of d rect and nd rect effects of IGCIP on speech, anguage, and read ng.

## PRELIMINARY STUDIES

**IGCIP.** Our image-guided approach to CI programming provides an automated electrode position analysis accounting for non-rigid variations in individualized cochlear anatomy. This requires a pre- and post-implant CT for all participants. Preoperative CT is considered standard of care for all CI recipients in the majority of CI programs and is thus available for all participants. Post-implant CT is also considered standard of care at Vanderbilt University Medical Center given the value-added information regarding electrode placement. Postoperative CT scans are obtained in the operating room immediately following implantation (preferred for pediatric CI recipients) or at subsequent clinical visits. We use a low radiation CT scanner (Xoran XCAT) (104,105) with ¼ of the radiation exposure of a typical head CT scan. Though we are using post-implant CT to identify extracochlear electrodes and overall electrode placement at Vanderbilt per standard of care, we are not yet applying IGCIP strategies in our clinical practice.

**Participants**. The impact of IGCIP has been assessed in 41 pediatric CI users for measures of spectral resolution, speech recognition, and quality of life. Children were 4.4 to 17.9 years (mean: 9.7 years) and all were provided with IGCIP and followed for 1 month up to 1 year. *A subset of these 41 participants (n=17) were assessed on measures of speech production and language both pre- and post-IGCIP.* None had confounding diagnoses such as autism spectrum disorder, neurological disorder, or general cognitive impairment.

**RESULTS: Speech recognition and auditory function.**

**Figure 5** displays speech recognition data in the experimental ear for 41 pediatric CI users with the IGCIP score plotted as a function of the baseline score obtained with the clinical CI program. The dashed lines represent the averaged 95% confidence intervals for monosyllabic words (106) and BabyBio sentences (107). Data points falling within the dashed lines represent no change in performance with IGCIP, points located above the top dashed line represent significantly better performance with IGCIP, and points located below the bottom dashed line represent significantly better performance with the standard clinical program. For speech recognition in quiet (monosyllables & sentences), 16% exhibited significantly better scores with IGCIP, 79% exhibited no change, and 5% demonstrated significantly poorer scores with IGCIP. For sentence recognition in noise, collapsed across signal-to-noise ratio (SNR), 28% exhibited significantly better performance with IGCIP, 69% exhibited no change, and only 3% exhibited significantly poorer performance with IGCIP. Considering the bilateral aided condition (i.e. IGCIP ear plus contralateral ear using either hearing aid or 2$^{nd}$ CI), *no child exhibited a significant decrement in speech recognition following IGCIP and 24% of the sample exhibited a significant improvement for sentence recognition in noise.* Auditory outcomes for an 18-participant subset of these 41 participants were published in Noble et al. (4). 31 of 41 children enrolled to date have elected to keep their IGCIP map for full-time use. In other words, though children are highly resistant to change, 76% of the sample opted to keep a novel program as compared to a program used for a range of 2 to 16 years prior to study enrollment—a testament to the perceptual benefits afforded by this intervention.

As displayed in **Figure 5**, many scores approached ceiling values for speech recognition in quiet and some even for speech recognition in noise with fixed SNRs (+10 and +5 dB). Thus we also administered a quasi-adaptive measure of sentence recognition in noise, the Bamford-Kowal-Bench Speech-In-Noise [BKB-SIN (108)] test. The BKB-SIN is a norm-referenced test [5 to 80 years (109)] yielding a score expressing the SNR required for 50% correct, and thus *lower scores represent better performance.* We obtained BKB-SIN data at baseline and following IGCIP for 19 of the 41 pediatric CI users [18 included in Noble et al. (4)]. For the IGCIP ear, 32% demonstrated significant IGCIP improvement, 63% exhibited no change, and just 1 (5%) exhibited significant IGCIP decrement. Mean BKB-SIN scores in the experimental ear were 13.0 and 11.8 dB at baseline and IGCIP, respectively. In the bilateral aided condition (IGCIP ear plus contralateral hearing aid or 2nd CI), no one exhibited IGCIP decrement and 37% of the sample exhibited a significant IGCIP benefit. Mean scores in the bilaterally aided condition were 8.2 and 6.8 dB at baseline and IGCIP, respectively.

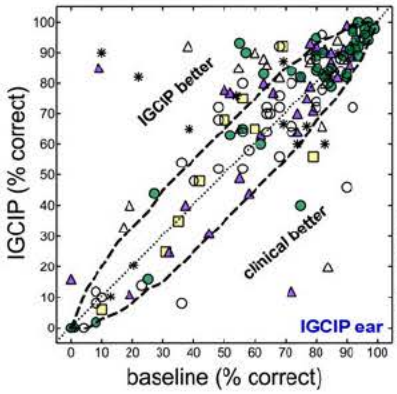



**Figure 5**

We followed 23 of the 41 children longitudinally for 1 year following enrollment. Children who kept the IGCIP map (n=16 or 70%) continued to demonstrate significant improvement in speech recognition at the group level ($p = 0.002$) 1 year following enrollment, and no one exhibited decrement in performance relative to baseline. The children who did not keep the IGCIP map (n=7 or 30%) either returned to baseline and maintained that performance for 1 year or showed minimal, non-significant improvement over the course of the year following study enrollment ($p > 0.05$). In other words, even children who rejected IGCIP for lack of benefit—or even exhibited short-term decrement—returned to baseline and maintained baseline-level performance following intervention. Thus we can conclude that IGCIP did not produce long-term harm for children not deriving benefit as well as children who demonstrated short-term decrement.

**Spectral and temporal resolution.** For 41 pediatric CI recipients, we found no relationship between spectral modulation detection (SMD) and speech recognition nor was SMD correlated with listener age ($r$ = -0.07 to 0.11; $p > 0.05$) (20). This finding is contrary to multiple reports for adult CI users as well as for our own data for which we found a significant correlation between SMD and various measures of speech recognition for 542 adult CI users (20). This suggests that pediatric CI users—with prelingual onset of deafness—may not be dependent on spectral resolution for high levels of speech recognition. ***In fact, we have pilot data for 14 pediatric CI users demonstrating a correlation between temporal modulation detection at 128 Hz and both monosyllabic word recognition ($r = -0.51$, $p = 0.05$) and sentence recognition in quiet ($r = 0.55$, $p = 0.04$).*** Furthermore, we have baseline and post-IGCIP data for 5 pediatric CI users showing a correlation between *IGCIP benefit* for monosyllabic word recognition and temporal modulation detection ($r = 0.94$, $p = 0.059$). These data are consistent with adult studies showing a significant correlation between temporal modulation detection and word recognition (59,110) and further motivate our hypothesis that pediatric CI users place greater weight on temporal vs. spectral cues.

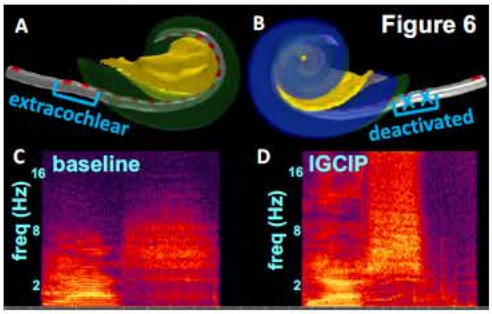



**Figure 6**

**Figure 6** displays data for a case study of a 4-year old CI recipient who demonstrated significant IGCIP benefit. **Figures 6A & B** display two views of the 3D reconstruction of the participant's cochlea with the implanted electrode array in place (green=scala tympani; blue=scala vestibuli; yellow=modiolus). The 2 most basal electrodes were found to be extracochlear. With these electrodes active in the CI map, the child was not receiving intracochlear stimulation for information above 4500-5000 Hz. Our IGCIP plan recommended deactivation of extracochlear electrodes (**Fig. 6B**), in addition to 1 electrode in the apical region based on calculation of intracochlear electrode-to-modiolus distance. By doing this, the incoming speech spectrum was reallocated to the remaining intracochlear electrodes transmitting information from 100 through 8500 Hz. Following IGCIP, this child exhibited a significant improvement in monosyllabic word recognition from 48% to 72% with just 6 weeks of IGCIP use; he did not, however, exhibit change on norm-referenced assessments of articulation. However, **Figures 6C** and **D** display spectrograms of his baseline and post-IGCIP production of the word "yes." After 6 weeks with IGCIP, he produced significantly greater higher frequency speech ($p < 0.001$) with greater amplitude in the /s/ region. Acoustic analyses also revealed significantly greater vowel precision ($t = 6.8$, $p < 0.0001$—articulatory vowel precision improving by more than a factor of 2). Despite

significantly greater speech energy > 3000 Hz following IGCIP (**Figure 6D**), there was no noted improvement in overall consonant precision nor consonant or vowel duration following IGCIP ($p > 0.05$). In contrast, we present a case study of a 6-year old CI user who did not demonstrate significant IGCIP benefit and in fact, showed slight decrement in monosyllabic word recognition with IGCIP (80% to 72%). However, this child exhibited a significant improvement in consonant precision (most pronounced for /j/, /h/ and /g/; $t = 4.2$, $p = 0.0001$) with an accompanying 30% increase in consonant duration following IGCIP. This child did not show any change in vowel precision nor vowel length. *This highlights the value of speech production and acoustic analyses in the context of this research proposal as we can track subclinical changes in speech production resulting from refinement of the CI signal.*

**PA.** The proposed measures of PA have been studied extensively by consultant Nittrouer and she has provided access to the paradigms she has employed in multiple studies of children with CIs. These measures have repeatedly been shown to predict language and reading in pediatric CI. In addition, Camarata has begun examining PA in children with hearing loss in the context of language, reading, and subjective fatigue and recently reported that standardized measures of PA predict language ability and reading skills (**Table 1**). Though consultant Nittrouer has more expertise in this area, PI Camarata also has experience and preliminary data on assessing PA in children with hearing loss that are directly relevant for the proposed research. These data also illustrate the analytic approach to be employed for these parameters in the proposed research.

**TABLE 1:** Regression Models or Phonological Awareness Receptive Language Reading Basic Skills[a] and Reading Comprehension[b] (adapted rom able 5 in Camarata et al in press)

| Model | $R^2$ adj | measure | B | SE B | β | t | p |
|---|---|---|---|---|---|---|---|
| 3[a] | 543 | Age | - 134 | 075 | - 175 | -1 793 | 079 |
| | | Nonverbal ntelligence | 467 | 150 | 325 | 3 110 | 003 |
| | | **Phonological Awareness** | **.544** | **.107** | **.509** | **5.073** | **.000** |
| 2[b] | 645 | Age | - 007 | 065 | - 010 | - 114 | 910 |
| | | Nonverbal ntelligence | 290 | 138 | 208 | 2 109 | 040 |
| | | **Reading—Basic Skills** | **.666** | **.097** | **.676** | **6.833** | **.000** |
| 4[b] | 745 | Age | - 037 | 056 | - 049 | - 655 | 515 |
| | | Nonverbal ntelligence | 125 | 122 | 089 | 1 021 | 312 |
| | | **Reading—Basic Skills** | **.412** | **.099** | **.099** | **4.152** | **.000** |
| | | **Reading—Receptive Lang** | **.401** | **.091** | **.091** | **4.388** | **.000** |

**Speech and language measures:** Speech and language tests administered for 17 of the pediatric IGCIP study participants included receptive language and speech using the Test of Auditory Comprehension of Language [TACL-3 (111)] and Goldman Fristoe Test of Articulation [GFTA-2 (112)], respectively. Correlations were computed for the raw gain scores on each test (note that "gain" could have been positive, negative, or 0) and the "benefit" scores from speech recognition tests quantifying IGCIP changes. The results are depicted in **Table 2** as correlation coefficients between BabyBio sentence recognition in noise at +5 and +10 dB signal-to-noise ratio (SNR) and TACL change scores (Δ) as well as GFTA change scores (Δ). Asterisks indicate significance. There were a number of significant correlations between IGCIP gain for speech recognition in noise and measures of receptive language and speech production. These results suggest that incidental gains in receptive language and speech production are associated with IGCIP benefit. This is an important clinical finding because it indicates that IGCIP can potentially benefit speech and language outcomes for pediatric CI recipients. The pediatric cases herein demonstrated speech and language growth that was proportional to the amount of benefit provided by individualized IGCIP and provide preliminary estimates of the effect sizes to power the proposed research.

| TABLE 2 | Δ TACL vocabulary | Δ TACL grammatical morphemes | Δ TACL elaborated sentences | Δ GFTA |
|---|---|---|---|---|
| BabyBio +5 dB | 0.12 | 0.31* | 0.20 | 0.28 |
| BabyBio +10 dB | 0.37* | 0.36* | 0.55* | 0.49* |
| BabyBio collapsed across SNR | 0.48* | 0.57* | 0.21* | 0.30* |

## APPROACH

Our **1st aim** is to compare pre- and post- IGCIP spectral and temporal resolution as well as word and non-word repetition (113,114) for pediatric CI recipients. Our **2nd aim** is to explore the complex relationships amongst spectral and temporal resolution, speech recognition, PA, and reading outcomes. Our **3rd aim** is to compare pre- and post-IGCIP raw scores on standardized tests of receptive language as well as speech production of pediatric CI users as these relate to spectral and temporal resolution and speech recognition. Our hypotheses are: 1) improved intracochlear spatial selectivity afforded by IGCIP will result in significant positive gain in spectral and/or temporal resolution and the magnitude of this gain will be significantly associated with gains in auditory comprehension (word and non-word repetition in quiet and noise), controlling for baseline levels of working memory and speech recognition, 2) spectral and/or temporal resolution as well as speech recognition will be associated with gain (change) in speech recognition and PA and that these, in turn, will significantly predict reading ability, and 3) spectral and/or temporal resolution as well as speech recognition will be associated with gain (change) in speech production and receptive language. Although the aggregate assessment protocol appears ambitious, with the exception of the PA, working memory, and the full complement of acoustic analyses, all procedures have been completed in children in our pilot and preliminary studies (4,20) and Camarata et al. (77) administered a more extensive battery (including standardized measures of PA) in 56 children with mild-to-moderate hearing loss, documenting feasibility of the proposed procedures.

**Participants.** The participants will be 60 pediatric CI recipients between the ages of 6 and 12 years. This age range was chosen as it is crucial for the development of speech, language, and literacy [e.g., (5)] and because 32 of the 41 participants (78%) in our preliminary studies were in this range and all were able to complete the proposed auditory test battery. Additionally, all measures of speech, language, PA, working memory, and literacy are routinely completed in this age range and have age normative data. Note that as 6- to 12-year olds are relatively consistent responders to the testing procedures herein, the reliability coefficients are >0.90 according to the test manuals; thus the SEM of these scores will be relatively narrow. None of the participants will have confounding diagnoses such as autism spectrum disorder, neurological disorder, or general cognitive impairment. Children must have at least one CI, < 3 years of age at implantation, and bilateral sensorineural hearing loss. Comprehensive audiological testing will be completed with all children as will the speech, language, PA, and reading assessments. We will collect and store child and family variables known to influence hearing, speech, and language outcomes such as chronological age at assessment, age at CI, age at identification, etiology, CI daily wear time [via datalogging (115,116)], nonverbal cognition, gender, maternal level of education, socioeconomic status, family size, and preschool educational environment [i.e. mainstream preschool, parent-infant program, listening and spoken language (10,15,117,118)].

**Design Overview.** The proposed research is a relatively straight-forward, double blind, waitlist controlled RCT. The *total initial sample* (n=72) will be randomly assigned to either immediate IGCIP intervention (n=36) or a deferred waitlist condition (n=36). Both groups will be monitored for 24 months (**Table 3**), with testing at time 1 (baseline), time 2 (2 months), time 3 (6 months), and time 4 (12 months). After 12 months, the deferred treatment group will receive the IGCIP intervention and testing will then continue *for both groups* at time 5 (14 months), time 6 (18 months), and time 7 (24 months). At completion, we will have 12 months of data on untreated growth, 12 months of treated growth in the deferred group, and 24 months of growth in the immediate IGCIP group. Note that "growth" can be positive, negative or neutral within in this design. Importantly, a between-group comparison of treated and untreated growth will be completed for data collected at 12 months. The study also permits comparison of growth at 24 months between groups (immediate vs. deferred treatment), which provides strong testing of IGCIP intervention effects.

| TABLE 3 | Baseline | 1 mo** | 2 mo | 6 mo | 12 mo | 13 mo** | 14 mo | 18 mo | 24 mo |
|---|---|---|---|---|---|---|---|---|---|
| Spectral, temporal, & spectrotemporal res | x | | x | x | x | | x | x | x |
| Speech rec | x | x | x | x | x | x | x | x | x |
| Subjective questionnaires | x | | x | x | x | | x | x | x |
| Speech production | x | | x | x | x | | x | x | x |
| Working memory, language, non-verbal cognition, PA, & literacy | x | | | | x | | | | x |

**SmartPhone app at home

We will ensure optimization of CI mapping including CI-aided thresholds in the range of 20 to 25 dB HL from 250 through 6000 Hz (119,120) as well as verification of upper stimulation levels via electrically evoked stapedial reflex thresholds (ESRTs) (121–123). For unilateral CI users with a hearing aid in the non-CI ear, we will verify hearing aid settings via real-ear measures (124). If clinical CI mapping was not completed per this protocol, we will program the child's CI and wait at least 2 months prior to completing a baseline assessment. If middle ear status does not allow ESRT measurements (e.g., effusion and/or PE tubes), upper stimulation levels will be obtained behaviorally, per clinical protocol. We will also complete thorough listening checks and test external equipment for signs of malfunction at every study visit.

**Procedures**

**IGCIP.** IGCIP provides an automated electrode position analysis accounting for non-rigid variations in individualized cochlear anatomy requiring pre- and post-implant CT for all study participants. Pre- and post-operative CT scans are considered standard of care treatment for all CI recipients at Vanderbilt given the electrode information provided by the image-guided analysis. We will define the electrode-to-modiolus interface by calculating distance-versus-frequency curves and then implementing a minimum error neural network to determine which electrodes for which their local minima (shortest electrode to modiolar distance) would be completely encompassed by adjacent electrodes. The goal is to maximize the number of active electrodes [>8 electrodes (125,126)] but also eliminate electrodes providing "redundant" electrical stimulation (i.e. channel interaction) or extracochlear electrodes. With IGCIP deactivation, we hypothesize a reduction in channel interaction which should increase spatial selectivity, and hence spectrotemporal resolution and speech recognition in noise. For bilateral CI users, IGCIP will be implemented for just 1 CI, targeting the poorer performing ear or the 2$^{nd}$ CI ear in the absence of interaural performance differences. This has been the IGCIP approach for all previous studies (4,71,127) and offers built-in control of the non-IGCIP ear as well as the bilateral CI condition (also see data presented in *Preliminary Studies*).

**Spectral, Temporal, and Spectrotemporal Resolution.** All tasks of spectral, temporal and spectrotemporal resolution will utilize a 3-interval, 2-alternative forced-choice procedure with broadband noise (125 to 8000 Hz) presented at 65 dB SPL in the sound field. For spectral resolution, the participant will be

asked to discriminate between noises with a flat spectrum and those with spectral modulation at rates of 0.5 and 1.0 cyc/oct—these rates have been shown to be significantly correlated with various measures of speech recognition (60,61,128). Temporal resolution will be assessed using amplitude modulation detection tasks in which the listener is asked to discriminate between noises with a flat temporal envelope and those with sinusoidal amplitude modulation at rates of 4, 32, and 128 Hz. These rates were chosen to define the plateau of the temporal modulation transfer function (4-32 Hz) as well as the sloping portion of the function (128 Hz) [e.g., (129)]. 4 Hz is also highly relevant for speech as it represents the peak modulation rate of the speech envelope modulation transfer function (130). Temporal modulation threshold will be expressed in 20 log m (dB), where m is the modulation index (0 to 1). Spectrotemporal resolution will be assessed using a stimulus with both spectral (1 cyc/oct) and temporal modulation (4 or 32 Hz) (131). Spectrotemporal modulation thresholds will be expressed in spectral modulation depth (dB) for each of the temporal modulation rates. For all measures we will use a 2-down, 1-up tracking procedure to track 70.7% (132). For all tasks, cartoon images of an animal are time locked with the auditory stimulus and displayed on a touchscreen monitor. The child is asked to identify which interval was “different” and responds via touchscreen display. We include auditory and visual feedback throughout the experiment with the goal of maintaining the child’s interest in the task. We have experience administering and interpreting these tasks in this age range as discussed in *Preliminary Studies*. *No prior study has described longitudinal auditory function for spectral, temporal, or spectrotemporal resolution in pediatric CI users in this age range within the context of an intervention-based RCT.*

**Speech Recognition.** We will assess speech recognition in each CI ear alone as well as the bilateral aided condition (bilateral CI or CI plus contralateral hearing aid) including monosyllabic words, non-words, as well as sentences in quiet and co-located noise (+5 dB SNR) with speech presented at 60 dB SPL in quiet and 65 dB SPL in noise. We will use CNC (106) monosyllables, non-word repetition tasks (114,133), BabyBio sentences (107) presented in quiet and at +5 dB SNR, as well as the BKB-SIN test (108). We will also obtain an adaptive speech receptive threshold for HINT sentences (134) presented at 0 degrees with semi-diffuse noise originating from 45 to 315 degrees as described in our previous publications (1,2). The semi-diffuse noise will be fixed at 72 dB SPL [typical restaurant noise level (135,136)] and the HINT sentences will be varied adaptively to yield 50% correct. *CNC, BabyBio, and BKB-SIN are all recommended by the Pediatric Minimum Speech Test Battery* (3) *and thus hold high clinical relevance.* Further, all measures have a sufficient number of lists allowing for longitudinal administration without repetition. We chose an SNR of +5 dB for fixed SNR assessment given that children aged 6-12 years spend ~80% of their day in noise including classrooms, school cafeterias, and playgrounds (137) and +5 dB is representative of the mean SNR encountered in everyday environments for elementary school-aged children (114-117). The additional measure of non-word repetition should be more sensitive to manipulations of IGCIP spatial selectivity and subsequent spectral resolution as non-words do not hold lexical meaning (114,139). Despite the ubiquity of the speech recognition measures, *there are no published data documenting the longitudinal performance trajectory for these measures of speech recognition and thus these data offer high clinical value.*

We will use a SmartPhone app to assess word recognition at the baseline and 12-month visits via Bluetooth or direct audio input. One month following baseline and 12-month visits, a caregiver will re-administer this test at home. In the event that word recognition has significantly declined relative to the immediately preceding visit—using 95% confidence intervals for test-retest variability of word tasks (140)—we will offer the option of returning the child to her previous CI map or giving an additional month with follow-up at the next scheduled appointment (at either 2 months or 14 months, per **Table 3**). Neither participant nor experimenter will not know whether the child is in the immediate IGCIP or waitlist deferred group. Should the child be withdrawn from the study due to negative outcomes, this will require that we break the blind for a given participant (see *Data Safety and Monitoring Plan*); however, we would continue to study auditory, speech, PA, language, and reading outcomes over a 2-year period for this child. *This will allow us to investigate underlying mechanisms responsible for those that are IGCIP responsive (estimated at over 75% of enrolled participants) as compared to non-responders—an important research question for clinical translation of this technology.*

**Subjective questionnaires (Auditory Skills & Quality of Life).** We will obtain subjective reports of auditory skills as well as overall quality of life for our pediatric participants using validated questionnaires: Auditory Skills Checklist [ASC (141)], Parents’ Evaluation of Aural/oral performance of Children [PEACH (142)], and Pediatric Quality of Life Inventory [PedsQL 4.0, (143)].

**Language Ability.** Language ability will be measured at two levels: expressive and receptive. Additionally, estimates of each domain will have multiple measures including vocabulary, morphology, and syntax. Receptive language abilities will be measured using the Receptive One-Word Picture Vocabulary Test-

4 [ROWPVT-4 (144)], Peabody Picture Vocabulary Test-4 [PPVT-4 (145)], and the TACL-4 (146) which includes separate subscale scores for vocabulary, morphology, and elaborated sentences. The receptive composite of the Clinical Evaluation of Language Fundamentals-4 [CELF-4 (147)] will also be administered to all participants. Expressive language will be measured using the Expressive One-Word Picture Vocabulary Test-4 [EOWPVT (148)], the Structured Photographic Expressive Language Test-3 [SPELT (149)], and the expressive composite on the CELF-4 (147).

**Speech production (standardized assessment and acoustic analyses).** Because children with hearing loss potentially display clinical speech disorders as well as subclinical speech alterations that can be detected only within the context of acoustic analysis, we will complete both standardized clinical measures and acoustic analyses. Traditionally speaking, due to the large amount of time spent on hand-analyses of speech production, a single dependent acoustic measure is chosen 'a priori'. This is often performed on a norm-referenced test of articulation such as the GFTA-3 (150), which we plan to administer; however, we will also supplement the GFTA-3 with acoustic analyses of speech samples obtained at each visit. The value of an objective speech acoustic analysis is that a very large number of measures can be computed with no subjective input thereby allowing us to investigate acoustic measures, or clusters of acoustic measures, that are related to the independent variable, i.e. implementation of IGCIP. We audio record the administration of the Renfrew bus story (151) as well as asking the child to repeat the Ling 6 sounds and "Twinkle Twinkle Little Star". We will obtain these speech samples at baseline and all subsequent study visits (**Table 3**). We will use Aural Analytics software (152) to obtain automated measures of 1) vocal quality (i.e. harmonic-to-noise ratio), 2) pitch ($F_0$: mean, stdev, range), 3) articulatory control [articulatory entropy (153)]; the envelope modulation spectrum; formant frequencies for consonants and vowels, vowel space; long-term average spectrum; speaking rate), and, 4) nasality (energy < 500 Hz). The algorithm for measuring articulation precision was calibrated using over 1000 hours of native English speech for adults and children and used to generate a normative distribution. In addition, we will manually investigate: a) differentiation between voiceless postalveolar affricates /ch/ and voiceless alveolar stop /t/—looking at peak amplitude and spectral mean of the fricative portions, b) differentiation of alveolar and postalveolar voiceless fricatives (/s/ vs /sh/), c) whole-word variability, and d) presence of atypical error patterns.

**Nonverbal assessment of cognition.** Nonverbal cognition will be assessed using the 3rd edition of the Leiter International Performance Scale [Leiter-3 (154)]. This is a standardized nonverbal estimate of cognitive abilities and was successfully administered with the participants in our pilot studies. All participants must exhibit nonverbal cognitive abilities within the typical range for inclusion. Should we identify a child exhibiting nonverbal cognitive abilities below the age-normative cutoff, we will refer to the developmental psychologist on the Vanderbilt CI Team.

**Working Memory.** Three tasks will be used: 1) Numbers Reversed from the Woodcock-Johnson IV (155) is a traditional test of memory span in which the child hears progressively longer strings of numbers and recalls in backwards order. Numbers will be audiorecorded with calibration and normalization of level (in dB SPL) for standardized auditory presentation across all participants and visits. Children will be asked to repeat each number prior to testing to ensure accurate recognition. 2) A serial recall task will be used to assess one's ability to use phonological structure to store words in a working memory buffer. This task has been used frequently, including pediatric CI users (75,76). The child sits in front of a touchscreen monitor and hears a string of 6 non-rhyming consonant-vowel-consonant, high-frequency nouns. After presentation, pictures of the 6 items appear on the display and the child is asked to touch the pictures in the order heard. The same 6 words are used across all trials and word recognition is confirmed both before and after testing. The serial recall task is used as it is more sensitive to phonological coding than free recall (156). 3) A visual-spatial task will be used, to assess working memory in the absence of verbal material. In this task, the touchscreen monitor is divided into 6 squares, and squares illuminate one at a time. The child is asked to tap on the squares in the order recalled. Reasons for using all three tasks of working memory are as follows: 1) The 1st task is a standardized task and will provide standardized scores that can be interpreted according to age norms and provide W scores, which are weighted raw scores that yield an estimate of ability level independent of age. 2) The 2nd task will assess children's abilities to use phonological structure in service to verbal working memory. Research has shown this task to be especially sensitive to differences in verbal working memory between children with NH who have typical language abilities and either children with CIs (referenced above) or children with NH, but phonological deficits (157). 3) The 3rd task will assess whether the participants have working memory deficits extending beyond simple verbal material.

**PA.** As with speech and working memory, we include standardized measures of PA as well as additional in-depth measures (developed in consultation with Dr. Nittrouer). PA is defined as the ability to

segment, discriminate, and operate on phonological units [speech sounds; see (158)]. The Comprehensive Test Of Phonological Processing [CToPP-2 (159)] is a norm-referenced and widely used standardized assessment of this ability and in our preliminary study of PA in children with hearing loss (94). To obtain multiple standardized estimates of PA, we will also administer the Test of Auditory Processing Skills [TAPS-3 (160)]. Both of these tests have been used extensively in previous studies of PA including several with children with CIs (161). In addition, Nittrouer and colleagues have developed an individualized set of tasks designed to provide an in-depth assessment of PA (8). They have argued that in parallel to subclinical alterations in speech production, specific aspects of PA may also illuminate the relationship between impoverished and/or altered access to the auditory CI signal and key aspects of PA. Because of this, in addition to the CToPP and the TAPS, we will also be administering the PA battery designed and studied in detail by Nittrouer including: Non-word Repetition, Initial Consonant Discrimination (Same-Different), Initial Consonant Choice, Final Consonant Choice, Phoneme Deletion, and Backwards Words (21). Although many of these tasks are sub-items on the CToPP and/or the TAPS, the in-depth PA battery includes multiple items that are developmentally ordered in each of these domains so that we can 1) accurately identify functional level for each skill at intake and 2) have sufficient sensitivity to capture short-term growth on one or more of these skills. Because there has been considerable variability in the relationships between speech recognition and PA in this population, we hypothesize that the IGCIP data will yield insight into the relationship between speech recognition, PA, and reading ability as well as receptive language with a specific focus on bootstrapping of PA.

**Reading Ability.** Reading ability includes two key factors, decoding and reading comprehension (162); we will obtain multiple measures of each of these factors. Standardized tests include the Woodcock Reading Mastery Tests [WRMT$^{TM}$-III (163)] and the Gray Oral Reading Test-5 [GORT-5 (164)]. Both instruments have been widely used with typically developing children and children with disabilities and, as with PA, have been applied to children with hearing loss in several studies. The WRMT$^{TM}$-III includes decoding assessments (e.g., letter word identification) and assessment of reading comprehension (e.g., Passage comprehension). Similarly, the GORT-5 includes estimates of decoding and reading comprehension including reading vocabulary comprehension and passage comprehension.

## STATISTICAL ANALYSIS PLAN AND POWER ANALYSES

**Scientific Rigor and Reproducibility and Data Management.** Dr. Dietrich (Co-I and biostatistician) will provide support for statistical analyses. All data will be stored in REDCap offering a secure, web-based application. All data analyses and data sharing will adhere to the NIH's commitment to rigorous and transparent research. This will be accomplished through the analytic approach described here, which replicates our previous analytical approaches used for studies of adult IGCIP (24,71) and our preliminary study of pediatric IGCIP (4). To achieve transparency, methodological details and raw data will be provided in our publications (data via sharing and/or supplements) that allow other research teams to reproduce the results.

**Statistical Analysis.** Statistical software (SPSS, STATA, R) will be used for the quantitative summarization of data and to test study hypotheses. The reliability of each of the scores from the standardized measures will be assessed and evaluated using Cronbach's alpha statistics. All analyses will be done using *intent-to-treat* principles. Statistical significance tests will maintain Type I error rates of no more than 0.05. Descriptive statistics will summarize and inspect the distributions of study measures for choosing the appropriate modeling procedure for testing hypotheses. See *Statistical Analysis Plan and Power Analyses* for a tabular summary of aims, hypotheses, and associated statistical models.

***Missing data***. Randomly missing responses to items within assessment tools will be handled via protocols specified by the instrument developers. When there is no protocol, if the participant has completed 75% or more of the items on a particular instrument, the mean score for that instrument will be calculated using available item responses and used in subsequent analyses. In-depth investigations of patterns of missing data will be undertaken to assess if data are missing due to random influences or if there are certain study conditions (e.g. waitlist control) or participant characteristics (e.g., age, hearing function) that are more or less likely to be associated with certain patterns of missing data (i.e. lost to follow-up). We expect that most assessments will not be missing at random, thus imputation would not be required.

***Aim 1 and Aim 2: Analysis & hypotheses testing:*** The outcome variables are auditory, speech recognition, PA, and reading gains over various time points (**Table 3**). Descriptive and graphical summaries of trajectories by study group will be conducted initially for detection of outliers and to provide insight into patterns of change. Key statistical tests will involve study group (immediate IGCIP vs. waitlist control) comparisons of the mean slopes resulting from differences in baseline and post-intervention assessments. Tests will be conducted using general linear mixed or multilevel analysis. While randomization ensures equal opportunity for

study conditions, it does not ensure equivalence of baseline values. To control for differences in opportunity for change from baseline and known impact of working memory, the respective measure baseline speech recognition and working memory will be included as covariates in the analysis. Within this general multilevel statistical approach, hypothesized differences will be tested by assessing the statistical significance of the main and interaction effects of study group on *time-related contrast* in baseline and post-baseline assessment points in the outcome variable scores. In other words, we expect that the slope of outcome measure scores in the waitlist control group will be nearly '0' while those of immediate IGCIP group will demonstrate a statistically significant positive slope. In addition to statistical significance testing, bootstrapping methods will be used to generate 95% confidence intervals for all sample descriptive (e.g., group means at each assessment) and effect estimates (e.g., $\eta^2$ for group effect on linear slope of outcome scores). Because we expect there to be correlations amongst the multiple outcome measures, a multivariate approach will provide more unified (systemic) statistical test of the intervention effects.

***Aim 3: Analysis and hypothesis testing:*** We will explore the complex relationships amongst changes in the various measures of hearing, speech, and language. **Figure 7** displays an example cross-lagged panel analysis which illustrates the structure for statistical analysis of this aim. Analyses comparing the strength of the relationships between the changes in one domain from baseline to 6-months with the changes in another domain from 6-months to 12-months will maximize the information gained from the longitudinal assessment of the multiple domains and enable us to draw some tentative causal hypotheses for subsequent research. Bootstrapped 95% confidence intervals will be generated for each of the path coefficients. For all statistical analyses, we will allow for covariates associated with the child and family including chronological age at assessment, age at implantation, age at identification, working memory, nonverbal cognition, gender, and socioeconomic status (6,11,97,98).

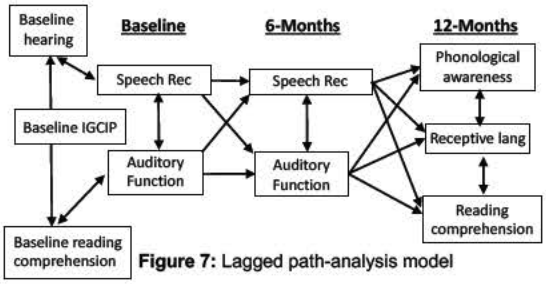


**Figure 7:** Lagged path-analysis model

***Sample size and power.*** Sample size estimates are based on the desire to detect clinically meaningful effects of the intervention using information from our preliminary studies while maintaining study feasibility. An analysis sample of 30 participants per study group will provide 80% statistical power (two-sided $\alpha$=0.05) for the detection of an intervention effect on the trajectories of the hearing, speech, language, PA and reading as small as 0.32 (Cohen's *d* equivalent=0.67, adjusted for baseline with $\eta^2 \geq 0.2$) and 0.35 (Cohen's *d* equivalent =0.74, unadjusted). Differences of this magnitude are considered to be clinically meaningful. Furthermore, the statistical power estimates are conservative due to the proposed used of mixed-effects analyses that will enable the increased power of treating the repeated assessments as independent values yet appropriately adjusting the standard errors for the correlations among those repeated assessments. The proposed final sample of 60 will enable detection of a path correlation as small as 0.35 (80% power, 2-tailed $\alpha$=0.05). Correlational values of that magnitude or larger were observed in our preliminary work. Detectable differences between the strength of two path coefficients will be 0.4-0.5 (80% power, 2-tailed $\alpha$=0.05) depending on the value of the coefficients and the size each correlation has with other values. The focus of the cross-lagged panel analysis will be on generating effect sizes deepening our understanding of the mechanisms underlying effects of change in hearing on higher-level PA/speech/language downstream. Accounting for 20% attrition, we will enroll 72 patients to achieve a 60-subject sample.

## POTENTIAL PROBLEMS AND ALTERNATIVE STRATEGIES

We anticipate that some participants will not complete all assessments at all time points, so that there will be incomplete data for some participants; we will employ statistical bootstrapping to handle missing data. We also anticipate that our personalized IGCIP plan could be identical to the clinical programming plan. This outcome is unlikely, (occurring in 5 cases out of over 200 participants thus far). If this occurs, the participant will be withdrawn from the study by the PIs because there would thus be no IGCIP "intervention" to investigate. It is also possible that we may find that the IGCIP method does not yield measureable improvement for a given participant or may even yield a decrement in performance. Based on our extensive experience working with this population, we have found that should a decrement in performance be observed, we will restore the patient's previous clinical settings and observe a return-to-baseline performance; additionally, we intend to assess word recognition 1 month following both potential intervention time points (1 month and 13 months) from home via SmartPhone to monitor for this possibility. Based on our preliminary data, only 7% of participants exhibited a short-term decrement in word recognition in the CI ear and none exhibited significant decrement in the bilaterally aided condition (i.e. bilateral CI or CI plus contralateral hearing aid).

# PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

| | |
|---|---|
| Are Human Subjects Involved | ● Yes ○ No |
| Is the Project Exempt from Federal regulations? | ○ Yes ● No |
| Exemption Number | ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8 |
| Other Requested Information | |

**Human Subject Studies**

| Study# | Study Title | Clinical Trial? |
|---|---|---|
| 1 | Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy | Yes |

## Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

1.1. Study Title *

Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy

1.2. Is this study exempt from Federal Regulations * ❍ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

| | | |
|---|---|---|
| 1.4.a. Does the study involve human participants? | ● Yes | ❍ No |
| 1.4.b. Are the participants prospectively assigned to an intervention? | ● Yes | ❍ No |
| 1.4.c. Is the study designed to evaluate the effect of the intervention on the participants? | ● Yes | ❍ No |
| 1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome? | ● Yes | ❍ No |

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

## Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- Image-Guided Cochlear Implant Programming (IGCIP)

2.2. Eligibility Criteria

Inclusion Criteria

1. children aged 6 to 12 years of age
2. prelingual onset of deafness
3. at least one CI and bilateral moderate to profound sensorineural hearing loss
    - for children with a single CI, audiometric thresholds in the non-CI ear must be consistent with at least a moderate to profound sensorineural hearing loss
4. cochlear implantation prior to 3 years of age
5. nonverbal cognitive abilities within the typical range
6. no confounding diagnosis such as autism spectrum disorder, neurological disorder, or general cognitive impairment
7. pre-operative CT scan of head performed as standard of care CI work-up
8. post-operative CT scan--obtained either before enrollment (per VUMC CI program standard of care) or after informed consent

Exclusion Criteria:

1. severe anatomical abnormality(s) of the temporal bone.
2. onset of moderate-to-profound sensorineural hearing loss after 2 years of age
3. nonverbal intelligence standard score < 85

| | | |
|---|---|---|
| 2.3. Age Limits | Min Age: 6 Years | Max Age: 12 Years |
| 2.4. Inclusion of Women, Minorities, and Children | S1-1_InclusionOfWomenAndMinorities.pdf | |
| 2.5. Recruitment and Retention Plan | S1-1_RecruitmentAndRetentionPlan.pdf | |
| 2.6. Recruitment Status | Not yet recruiting | |
| 2.7. Study Timeline | S1-1_StudyTimeline.pdf | |
| 2.8. Enrollment of First Subject | 11/01/2018 | Anticipated |

## INCLUSION OF WOMEN, MINORITIES AND CHILDREN

*Women*
No subject will be excluded from participation due to gender or race. The investigators will be blind to race and ethnicity of participants prior to enrollment. Since all patients aged 6 to 12 years with bilateral sensorineural hearing loss and at least one cochlear implant will be targeted for recruitment. No data exist regarding demographics of pediatric cochlear implant (CI) candidates making it difficult to anticipate the ethnic composition of this study. However, based on participation demographics of previous studies an equal mix of male and females is likely.

*Minorities*
As stated in the Human Subjects and Approach sections of this application, we will post IRB approved recruitment fliers in the waiting room of the VUMC Audiology and ENT clinics as well as in the adult CI programming rooms to recruit experienced adult participants. **Every effort will be made to recruit minorities for participation.** To facilitate this, we will make use of the Vanderbilt Kennedy Center's Core Research Support Services for assistance with participant recruitment. This core is supported by NICHD Grant P30 HD15052 to the Vanderbilt Kennedy Center for Research on Human Development. This core service provides investigators with access to databases for recruitment purposes, and easy access to large-scale, statewide, linked administrative databases on demographics and health related variables (e.g., birth death, marriage, hospital discharge) for pilot testing and research purposes.

The attached **Targeted/Planned Enrollment Form** reflects data obtained from the Vanderbilt University CI lab database of implant recipients for whom we have documented ethnic and racial categories. As previously mentioned, there are no published studies documenting the demographics of pediatric cochlear implant candidates which makes the task of ensuring adequate representation of ethnic and racial categories difficult. However, based on the limited data we have in the VUMC CI program database of pediatric implant recipients as well as a recently published paper describing racial and ethnic composition of our adult CI candidates at Vanderbilt [Holder JT, Reynolds SM, Sunderhaus LW, Gifford RH (2018). Current Profile of Adults Presenting for Preoperative Cochlear Implant Evaluation. Trends Hear, 22: 1-16], we expect that the ethnic and racial diversity of the recruited participants for this study *to be different* from that of the greater Nashville metropolitan areas. Thus the **Targeted/Planned Enrollment Form** reflects our *expected enrollment* with respect to ethnic and racial diversity.

*Children*
The participants involved in this proposed research are children, ranging in age from 6 to 12 years at the time of testing. All children will have at least one cochlear implant and bilateral sensorineural hearing loss. This age range has been chosen based on our preliminary studies as children in this age range will be able to complete all proposed auditory, speech, language, and literacy assessments, as well as the subjective reports of listening behaviors and overall quality of life.

The PIs, Drs. Gifford and Camarata, are an audiologist and speech language pathologist, respectively. Both PIs have decades of experience working with children in both clinical and research settings. The Cochlear Implant Research Laboratory and the Developmental Disabilities Laboratory are both well-equipped and designed to accommodate pediatric research participants and their families.

## RECRUITMENT AND RETENTION PLAN

Patients will be recruited from the CI program at Vanderbilt University Medical Center, one of the largest programs in the United States, with an average of 250 CI recipients annually (65% adult) and over 3000 recipients since inception in 1996. Over the duration of the study, We anticipate enrollment of 72 study participants to achieve our target sample size of 60 completed participants (30 in each group). Each year we implant approximately 60 pediatric CI patients. An analysis of all pediatric CI recipients implanted at Vanderbilt University Medical Center from January 2011 through December 2017 revealed that we have 206 pediatric CI recipients aged 6 to 12 years of age with prelingual onset of bilateral moderate to profound sensorineural hearing loss, who were younger than 3 years of age at implantation. However, there are multiple additional prospective participants who will reach the age-related criteria over the course of the project. Informed consent and assent will take place as per our institution’s IRB policies and be obtained by the PIs, co-Is, and/or other appropriately trained member of the research team using an IRB-approved consent form. Retention will be promoted by providing the parents and children with detailed information regarding their performance on various tasks of auditory processing, speech recognition, speech production, language, and literacy. Following each study visit, we will compile a report of each child’s performance to be mailed to the child’s home address on file. Study participation will provide value-added information regarding a variety of auditory, speech, language, and literacy tasks that are not typically included in clinical appointments.

## STUDY TIMELINE

Both study groups will be monitored for 24 months, with testing at time 1 (baseline), time 2 (2 month), time 3 (6 month), and time 4 (12 month). At the 12-month visit, the deferred treatment group will receive the IGCIP intervention. Testing will then continue *for both groups* including time 5 (14 month), time 6 (18 month), and time 7 (24 month). At the conclusion of the project, we will have 12 months of data on untreated growth for the deferred group, 12 months of treated growth in the deferred treatment group, and 24 months of treated growth in the immediate intervention group. Detailed plans for the study timeline are provided in the table below.

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 |
|---|---|---|---|---|---|
| **Months 1-3** | • Hire and train full-time project manager (including RCR principles)<br>• Enroll and train PhD student on methods, data collection, and RCR principles (ongoing instruction)<br>• Purchase assessment materials<br>• Verify study details posted to clinicaltrials.gov<br>• Initial videoconferencing with consultants Drs. Nittrouer and Bunta<br>• Active recruitment to enroll large number of participants in next 3-month period<br>• Obtain randomization schedule from Dr. Dietrich<br>• 3 monthly project meetings will be held | • Ensure human subjects training and RCR annual course is completed for all study personnel<br>• Study visit 3 (6 months post baseline) should be completed for all participants enrolled in Year 1, months 7-9<br>• Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 1, months 4-6<br>• Active recruitment for enrollment in the next 3-month period<br>• 3 monthly project meetings will be held<br>• Drs. Nittrouer and Bunta will visit Vanderbilt meeting with all study personnel | • Ensure human subjects training and RCR annual course is completed for all study personnel<br>• Study visits 5-7 completed for all participants enrolled & consented in year 1<br>• Study visit 3 (6 months post baseline) should be completed for all participants enrolled in Year 2, months 7-9<br>• Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 2 months 4-6<br>• Active recruitment for enrollment in the next 3-month period<br>• Drs. Nittrouer and Bunta will visit Vanderbilt meeting with all study personnel<br>• 3 project meetings<br>• Initial manuscript preparation commences describing spectral, temporal and spectrotemporal processing | • Ensure human subjects training and RCR annual course is completed for all study personnel<br>• Study visits 5-7 completed for all participants enrolled in years 1 & 2 and half of the participants enrolled in year 3<br>• Study visit 3 (6 months post baseline) should be completed for all participants enrolled in Year 3, months 7-9<br>• Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 3 months 4-6<br>• 3 monthly project meetings<br>• Videoconferencing with consultants Drs. Nittrouer and Bunta<br>• Manuscript submitted describing relationship between auditory perception and speech, language, and literacy | • Ensure human subjects training and RCR annual course is completed for all study personnel<br>• Study visit 4 (12 months post baseline) completed for all enrolled participants from Year 3<br>• Study visits 5-7 completed for all participants enrolled in years 1-2 and ½ participants enrolled in year 3<br>• Attend and present at HEAL 2022<br>• 3 project meetings |
| **Months 4-6** | •Active summer enrollment—school-aged children are on summer break (targeted recruitment and baseline assessment for ~ 12-14 participants by the end of month 6)<br>•3 project meetings | •Active summer recruitment—school-aged children are on summer break (targeted recruitment and baseline assessment for ~ 12-14 participants by the end of month 6)<br>•Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 1 months 7-9<br>•3 project meetings | •Active summer recruitment (targeted recruitment and baseline assessment for ~ 12-14 participants by the end of month 6)<br>•Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 2 months 7-9<br>• Study visits 5 (14 months), 6 (18 months) and 7 (24 months) completed for all participants enrolled in year 1, months 4-6 | •Study visit 4 (12 months post baseline) will be completed for ~ 7 enrolled participants from Year 3 months 7-9<br>• Verify that study visit 4 (12 months post baseline) is completed for all enrolled participants from Year 3 months 4-6<br>• 3 project meetings<br>• Attend & present at SRCD 2022 | • Study visit 4 (12 months post baseline) completed for ~ 7 enrolled participants from Year 4 months 7-9 |

| | | | | | |
|---|---|---|---|---|---|
| | | | • 3 project meetings<br>• Attend and present at CIAP 2021 | | |
| **Months 7-9** | • Study visit data obtained from home administration of SmartPhone app 1 month following baseline and 2month visits will be completed for all enrolled participants to date<br>• Attend ASHA 2019<br>• Enroll ~5-6 new participants (winter break)<br>• 3 project meetings | • Study visit data obtained from home administration of SmartPhone app 1 month following baseline and 2-month visits will be completed for all participants enrolled in Year 2, months 4-6<br>• Attend & present at ASHA 2020<br>• Enroll ~5-6 new participants (winter break)<br>• Blinded data will be analyzed and abstract prepared for submission for American Auditory Society (AAS) 2021 as well as Conference on Implantable Auditory Prostheses (CIAP) 2021<br>• 3 monthly project meetings will be held | • Study visit data obtained from home administration of SmartPhone app 1 month following baseline and 2-month visits will be completed for all participants enrolled in Year 3, months 4-6<br>• Attend & present at ASHA 2021<br>• Enroll ~10 new participants (winter break)<br>• Study visits 5 (14 months), 6 (18 months) and 7 (24 months) completed for all participants enrolled in year 1, months 7-9<br>• Blinded data will be analyzed and abstract prepared for submission for American Cochlear Implant Alliance (ACIA) 2022, Hearing Across the Lifespan (HEAL) 2022, and SRCD<br>•3 project meetings | • Attend & present at ASHA 2022<br>• Study visits 5 (14 months), 6 (18 months) and 7 (24 months) will be completed for all participants enrolled in year 2, months 7-9<br>• Study visit 4 (12 months) will be completed for all enrolled participants from Year 3 months 4-6 and ½ participants enrolled in Year 3 months 7-9<br>• 3 project meetings | • Attend & present at ASHA 2023<br>• Study visits 5-7 will have been completed for all participants enrolled in years 1-3<br>• Upon completion of visit 7 for the last enrolled participant, the data will be unblinded allowing for the majority of the statistical analyses to be completed<br>• Active data analysis on unblended dataset<br>• Manuscript preparation on unblinded datasets spanning all aims and experiments<br>• 3 project meetings |
| **Months 10-12** | • Verify study visit 3 (6 months post baseline) is completed for all enrolled from months 1-6, Year 1<br>• Study visit 4 (12 months post baseline) scheduled or completed for ½ of enrolled participants (n = 7)<br>• Study data obtained from home administration of SmartPhone app 1 month following baseline and 2-month visits will be completed for participants enrolled in months 7-9<br>• Blinded data will be analyzed and abstract will be developed and | • Verify study visit 3 (6 months post baseline) is completed for all enrolled participants from months 1-6, Year 2<br>• Study visit 4 (12 months post baseline) completed for ½ of enrolled participants from Year 2, months 4-6 (n = 7)<br>• Study data obtained from home administration of SmartPhone app 1 month following baseline and 2-month visits will be completed for participants enrolled in Year 2, months 7-9<br>• Blinded data will be analyzed and abstract will be developed and submitted for ASHA 2021 on longitudinal auditory perceptual data<br>• Attend and present at AAS 2021 | • Verify that study visit 3 (6 months post baseline) is completed for all enrolled participants from months 1-6 in Year 3<br>• Study visit 4 (12 months post baseline) scheduled or completed for ½ of enrolled participants from Year 3, months 4-6 (n = 7)<br>• Study data obtained from home administration of SmartPhone app 1 month following baseline and 2-month visits will be completed for participants enrolled in Year 3, months 7-9<br>• 3 project meetings<br>• Preparation of Year 3 RPPR | • Study visit 4 (12 months post baseline) completed for ½ of enrolled participants from Year 3, months 7-9<br>• Verify that study visits 5 (14 months), 6 (18 months) and 7 (24 months) are completed for all participants enrolled through year 2, months 1-12<br>• 3 project meetings<br>• Preparation of Year 4 RPPR | • Active data analysis on unblinded dataset<br>• Manuscript preparation on unblinded datasets spanning all aims and experiments<br>• Preparation of Project RPPR<br>• NOTE: Given the longitudinal nature of this double-blinded RCT, we anticipate requesting a no-cost extension year to fully complete data dissemination via peer-reviewed manuscript submissions and presentation of unblinded data |

| | | | | | |
|---|---|---|---|---|---|
| | submitted for ASHA 2020 on longitudinal auditory perceptual data<br>• 3 project meetings<br>• Preparation of Year 1 RPPR | • 3 monthly project meetings<br>• Preparation of Year 2 RPPR | | | |

**Inclusion Enrollment Reports**

| IER ID# | Enrollment Location Type | Enrollment Location |
|---|---|---|
| Study 1, IER 1 | Domestic | |

## Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ❍ Yes ● No

Enrollment Location Type* : ● Domestic ❍ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s):

Comments: Estimated total enrollment over 5 year study. We anticipate enrollment of 72 study participants to achieve our target goal of 60 completed participants (30 in each group). The numbers shown below are for all 72 enrolled participants.

**Planned**

| Racial Categories | Ethnic Categories | | | | Total |
|---|---|---|---|---|---|
| | Not Hispanic or Latino | | Hispanic or Latino | | |
| | Female | Male | Female | Male | |
| American Indian/ Alaska Native | 0 | 0 | 0 | 0 | 0 |
| Asian | 2 | 2 | 0 | 0 | 4 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 | 0 |
| Black or African American | 3 | 3 | 0 | 0 | 6 |
| White | 27 | 27 | 2 | 3 | 59 |
| More than One Race | 2 | 1 | 0 | 0 | 3 |
| **Total** | 34 | 33 | 2 | 3 | 72 |

**Cumulative (Actual)**

| Racial Categories | Ethnic Categories | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | Not Hispanic or Latino | | | Hispanic or Latino | | | Unknown/Not Reported Ethnicity | | | |
| | Female | Male | Unknown/ Not Reported | Female | Male | Unknown/ Not Reported | Female | Male | Unknown/ Not Reported | |
| American Indian/ Alaska Native | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| White | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| More than One Race | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

## Section 3 - Protection and Monitoring Plans (Study 1)

| | |
|---|---|
| 3.1. Protection of Human Subjects | S1-1_ProtectionOfHumanSubjects.pdf |
| 3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site? | ❍ Yes ● No ❍ N/A |
| If yes, describe the single IRB plan | |
| 3.3. Data and Safety Monitoring Plan | S1-1_DataSafetyMonitoringPlan.pdf |
| 3.4. Will a Data and Safety Monitoring Board be appointed for this study? | ❍ Yes ● No |
| 3.5. Overall structure of the study team | S1-1_StudyTeamStructure.pdf |

## PROTECTION OF HUMAN SUBJECTS

### Risks to Human Subjects

### Human Subjects Involvement, Characteristics, and Design

We anticipate enrollment of 72 study participants to achieve our target goal of 60 completed participants (30 in each group).

The following inclusion and exclusion criteria will be used:

Inclusion Criteria:

- children aged 6 to 12 years of age
- prelingual onset of deafness
- at least one CI and *bilateral* moderate to profound sensorineural hearing loss
    - for children with a single CI, audiometric thresholds in the non-CI ear must be consistent with at least a moderate to profound sensorineural hearing loss
- cochlear implantation prior to 3 years of age
- nonverbal cognitive abilities within the typical range
- no confounding diagnosis such as autism spectrum disorder, neurological disorder, or general cognitive impairment
- pre-operative CT scan of head performed as standard of care preoperative CI work-up
- post-operative CT scan—obtained either before enrollment (per VUMC CI program standard of care) or after informed consent, if implanted elsewhere. Note that if an outside implanted participant is recruited for study participation, Co-I Dr. Labadie has an active IRB approved study—which will be linked to this study's IRB application—allowing for Xoran CT scanning of children aged 6 years and older. Six years of age is the youngest age for which this can be reliably completed given the need to sit completely still for ~15 seconds.

Exclusion Criteria:

- severe anatomical abnormality(s) of the temporal bone (e.g., common cavity, cochlear ossification)
- onset of moderate-to-profound sensorineural hearing loss *after* 2 years of age
- nonverbal intelligence standard score < 85

The study procedures that participants will undergo are provided in *Research Strategy: Approach*.

### Sources of Material

Data collected will consist of the following fields: age at each test point, gender, age at implantation, age at hearing loss identification, nonverbal cognition, gender, maternal education, socioeconomic status, family size, preschool educational environment (i.e., mainstream preschool, parent-infant program, listening and spoken language preschool), pre- and post-operative temporal bone CT scan (stored in centralized data repository), date of surgery, study group (blinded until study completion), device, electrode type (perimodiolar, lateral wall), angular insertion depth, date of post-operative activation of CI, device wear time (via datalogging), as well as all data specified in the Approach.

### Research Strategy: Approach

Data will not be individually identifiable but will be coded to mask participant identity with a master list kept by the PIs. Study data will be collected and managed using REDCap electronic data capture tools hosted at Vanderbilt. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. (Paul A. Harris, Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, Jose G. Conde, Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support, J Biomed Inform. 2009 Apr;42(2):377-81.)

**Potential Risks**
The investigation involves a new method of programming cochlear implants based on a comparison of pre- and post-operative CT scans. The risk to the patient is radiation exposure due to the postoperative CT scan; however, *we complete postoperative scanning routinely for all CI recipients at VUMC (unless declined by the patient) given that the information gained by the scan and image processing has been determined by the Vanderbilt CI team to offer significant clinical value to the patient for CI programming optimization (e.g., identification of extracochlear electrodes, tip foldover).* The other portions of the research–namely deactivating CI electrodes–are within the scope of practice of audiologists for CI programming and thus utilize CI clinical software that is FDA approved and regulated. Oversight for all study procedures will be provided by the Vanderbilt's Institutional Review Board and managed by the study PIs.

Regarding radiation risk, Vanderbilt has both traditional multi-slice CT scanners (MSCT) as well as flat-panel volumetric computerized tomography (fpVCT) machines. All machines are FDA-cleared for temporal bone CT scanning and undergo annual inspection from the Department of Radiology and Radiological Sciences, Division of Radiological Sciences per state regulations. Oversight will be provided by the Radiation Review Committee, part of Vanderbilt's Human Research Protection Program.

**Adequacy of Protection against Risks**

**Recruitment and Informed Consent**
Patients will be recruited from the CI program at Vanderbilt University Medical Center, one of the largest programs in the United States, with an average of 250 CI recipients annually (65% adult) and over 3000 recipients since inception in 1996. Over the duration of the study, We anticipate enrollment of 72 study participants to achieve our target sample size of 60 completed participants (30 in each group). Each year we implant approximately 60 to 80 pediatric CI patients. An analysis of all pediatric CI recipients implanted at Vanderbilt University Medical Center from January 2011 through December 2017 revealed that we have 251 pediatric CI recipients aged 6 to 12 years of age with prelingual onset of bilateral moderate to profound sensorineural hearing loss, who were younger than 3 years of age at implantation. However, there are over 220 additional prospective participants already being followed by our center who will reach the age-inclusion criteria over the course of the project. Informed consent and assent will take place as per our institution's IRB policies and be obtained by the PIs, co-Is, and/or other appropriately trained member of the research team using an IRB-approved consent form.

Study retention will be promoted by providing the parents and children with detailed information regarding their performance on various tasks of auditory processing, speech recognition, speech production, language, and literacy. Following each study visit, we will compile a report of each child's performance to be mailed to the child's home address on file. Study participation will provide value-added information regarding a variety of auditory, speech, language, and literacy tasks that are not typically included in clinical appointments.

**Protection Against Risk**
Patients will be closely followed for any adverse events related to the study through individual pre- and post- intervention visits. Any adverse events will be reported to the IRB according to each institution's policy and procedures.

The confidentiality of the patients will be assured through adherence to HIPAA guidelines. Results will be tabulated in a digitally maintained database as follows: (a) Data will not be individually identifiable but will be coded to mask participant identity, (b) A master list will be kept by the PIs, (c) Hard copies of data sheets will be stored in locked offices, (d ) Digital data will be stored on password protected computers, (e) Data will be kept for a minimum of 6 years after the research is complete, (f) Only research personnel will have access to the data.

**Data Safety Monitoring Plan**.
The PIs provide oversight of the study. The PIs will be responsible for recording and reporting adverse events to the IRB in a timely fashion according to institutional policies. To date, no adverse events have

been recorded for the 41 pediatric CI participants in the preliminary study. We will continue to follow all regulatory requirements including timely reporting of adverse events to our IRB, careful adherence to strict inclusion/exclusion criteria, and at least annual reporting of progress. Given the primary risk of the study is drop in speech recognition abilities for the experimental ear, we anticipate that our IRB will deem this a minimal risk study (as it has our preliminary study) which does not require a Data Safety Monitoring Board (DSMB). Should the IRB request a DSMB we will organize such from investigators within the Vanderbilt community who have no association with either the current study and/or the PI and co-I's. To accomplish this, we will utilize Vanderbilt's NIH-funded Institute for Clinical and Translational Research. Additionally, our team will continue to meet at least monthly (as we currently do) to update patient enrollment and address any concerns brought up by participants and/or members of the research team.

### 6.1.3 Potential Benefits of the Proposed Research to Human Subjects and Others

The potential benefits of the research are to improve outcomes for pediatric CI recipients. Our goal is to gain a better understanding of underlying mechanisms driving speech understanding for pediatric CI recipients and to investigate the This is done by deactivating individual electrodes which, based on geometric position determined by CT scanning, are interfering with neighboring electrodes. Our preliminary data show statistically significant improvement in audiological and quality of life metrics in long-term CI users. This study will investigate whether similar improvements are seen in a large group of pediatric CI recipients.

### Importance of the Knowledge to be Gained

If successful, IGCIP could become a preferred method of CI programming for pediatric CI recipients improving patient performance and satisfaction. Further, the knowledge of outcomes for children with CI on measures of speech understanding, speech production, language, and literacy at various time points with different audiologic intervention holds great empirical and as well as clinically translational relevance as these data are not widely available in the peer-reviewed literature.

## DATA AND SAFETY MONITORING PLAN

*Data Safety Monitoring Plan*. To date, no adverse events have been recorded for the nearly 300 adult and pediatric study participants who have been enrolled in our preliminary studies, thus far. We propose to continue to follow all regulatory requirements including timely reporting of adverse events to our IRB (within 10 days of the event), careful adherence to strict inclusion/exclusion criteria, and at least annual reporting of progress. Given the primary risk is radiation exposure secondary to the postoperative CT scan, we anticipate that our institutional review board (IRB) will deem this a minimal risk study (as it has with our preliminary studies) which does not require a Data Safety Monitoring Board (DSMB). In fact, all CI recipients at VUMC are already routinely scanned postoperatively because the CI clinical team has determined that the radiation risk is relatively low (i.e. equivalent to a cross-country airline flight) and the information to be gained is high for audiologic and otologic management of the CI recipient and optimization of CI programming. Because this project poses minimal risk and involves a single site, data and safety of the project will be monitored by the IRB at Vanderbilt University School of Medicine and the principal investigators of the project in conjunction with Dr. Labadie, who is an otologic surgeon in the VUMC CI program and Co-I on this project.

*Prospective assignment of one or more human subjects.* All participants will receive intervention; however, half of the participants will be randomly assigned to immediate intervention and the other half will be assigned to the deferred intervention group using a waitlist control study design. Randomization to IGCIP or waitlist IGCIP will occur after written informed consent and will proceed in the same way for both testing periods. As described in the Approach, we will be using identical procedures for all participants regardless of arm to which they randomize including generation of an IGCIP plan, and longitudinal assessments performed by an audiologist and speech-language pathologist.

A randomization schedule will be generated by Co-I and study statistician, Mary Dietrich, PhD, and provided to the PIs (Gifford and Camarata) prior to study commencement. To ensure equal numbers of participants in each arm, a computer-generated, permuted blocking algorithm (blocks of 4 participants) will be used to develop the schedule. The schedule will be password protected and saved on an encrypted server housed at the Vanderbilt Bill Wilkerson Center. As described in the Approach, we will be using identical procedures for all participants regardless of arm to which they randomize including (a) post-operative CT scanning, (b) generation of an IGCIP plan, and (c) longitudinal assessments performed by an audiologist and speech-language pathologist.

*Blinding.* Both the experimenters and the participants will be blinded. The experimenters will be notified of the randomization for a given participant on the day of the baseline visit. Only the PIs and Co-I Dr. Dietrich, who will generate the randomization scheme, will know whether the participant is in the intervention or deferred waitlist group until the end of the study. Neither PI nor Dr. Dietrich will be personally administering assessments nor scoring tests for the participants.

*Provisions for breaking the blind.* To ensure that IGCIP does not impair auditory-only word recognition—an important ethical control in this clinical trial—we will use a SmartPhone app, (e.g., Hear Coach) to assess word recognition during the respective baseline as well as at 1 month and 13 months following enrollment—as neither the participants nor the tester will know whether the subject is in the immediate or deferred intervention group. Words will be transmitted from the SmartPhone app via Bluetooth or direct audio input at a comfortable level. Study staff will administer the assessment at baseline; a caregiver will be asked to re-administer smartphone word task at home during the subsequent periods. In the event that word recognition has decreased relative to scores obtained during the previous study visit—using 95% confidence interval data for test-retest variability of word recognition tasks containing 25 items—we will offer the option of returning the child to a previous program or giving the child one additional month of study participation to be followed up at the regularly scheduled appointment for each group (Table 3). Note that it is possible that there will be some cases where no changes were made to the child's previous program for those in the deferred intervention. If no changes have been made to the child’s CI program—as in the case of the waitlist deferred group at the 1-month post enrollment appointment—we would not expect changes in word recognition. However, should there be an aberrant/unexplained change in the child’s hearing status and a change in word recognition *without a change to the CI*

*Evaluation of the effects of the intervention on one or more health-related biomedical or behavioral outcomes*
The evaluation of the intervention (IGCIP) will be assessed using various measures of basic auditory function (spectral and temporal resolution), speech understanding, speech production, language (expressive and receptive), phonological awareness, and literacy. We will also be tracking outcomes longitudinally on subjective measures of auditory function (ASC—completed by primary caregiver), communication in quiet and noise (PEACH—completed by primary caregiver), and PedsQL 4.0 (completed by both child participant and primary caregiver).

## OVERALL STRUCTURE OF THE STUDY TEAM

The proposed research is a collaboration between an audiologist (Gifford) and a speech language pathologist (Camarata) collaborating with an otologist (Labadie), engineers, (Labadie, Noble, Dawant), and a biostatistician (Dietrich). We have two external consultants, Susan Nittrouer, PhD and Ferenc Bunta, PhD who are experts in phonological processing and speech production, respectively. We will have a project manager who is yet to be identified. This project will be overseen by the PI's, Drs. Gifford and Camarata with input at monthly project meetings and regular ongoing interaction with our co-investigators, consultants, and project manager.

## Section 4 - Protocol Synopsis (Study 1)

4.1. Brief Summary

The proposed research is a relatively straight-forward, double-blind, wait-list controlled randomized clinical trial (RCT) design. The total sample (n = 72) will be randomly assigned to either immediate IGCIP intervention (n = 36) or a deferred waitlist condition (n = 36). Both groups will be monitored for 24 months, with testing at time 1 (baseline), time 2 (2 months), time 3 (6 months), and time 4 (12 months). After 12 months, the deferred treatment group will receive the IGCIP intervention. Testing will then continue at time 5 (14 months), time 6 (18 months), and time 7 (24 months). At the conclusion of the project, we will have 12 months of data on untreated growth, 12 months data of treated growth in the deferred treatment group, and 24 months of growth in the immediate IGCIP treatment group.

4.2. Study Design

4.2.a. Narrative Study Description

This project provides a unique opportunity to examine whether individualized, image-guided CI programming (IGCIP) significantly improves outcomes in pediatric CI patients. The proposed research activities will examine the impact of personalized IGCIP in pediatric patients on measures of basic auditory function (spectral and temporal processing), word and non-word recognition, speech production, language, phonological processing, and reading comprehension using a randomized wait-list control treatment design. A total sample of 72 children with CIs aged six to twelve years old will be enrolled in the project: half (n = 36) will be randomized to an immediate IGCIP condition and half to a 12 month waitlist control condition. The waitlisted participants (n = 36) will undergo IGCIP after 12 months of monitoring and then followed for an additional 12 months after the IGCIP intervention has been provided (total time in the study: 24 months). Those immediately provided with IGCIP will also be followed for a total of 24 months. All participants will undergo extensive audiological as well as speech, language, and reading assessments in addition to comprehensive audiological assessment at baseline as well as at regular intervals: 2, 6, 12, 14, 18, and 24 months. We will use predictor analyses to determine the impact of immediate and deferred IGCIP on subsequent auditory, speech, language, and literacy outcomes.

4.2.b. Primary Purpose: Treatment

4.2.c. Interventions

| Type | Name | Description |
|---|---|---|
| Other | Signal processing intervention of a biomedical device | This is a signal processing intervention of an FDA approved biomedical device for study participants that have received the cochlear implant based on clinical recommendations (i.e. not study related). Based on image processing of pre- and post-implant CT, cochlear segmentation, electrode scalar localization, and definition of the electrode-to-neural interface, we will manipulate the stimulus delivery of the incoming signal within the FDA approved clinical software and thereby is within the electrical and clinical specifications of the FDA approved device and accompanying software. |

4.2.d. Study Phase: Early Phase 1 (or Phase 0)

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ● No

4.2.e. Intervention Model: Sequential

4.2.f. Masking ❍ Yes ● No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation: N/A

4.3. Outcome Measures

| Type | Name | Time Frame | Brief Description |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Primary | Spectral resolution (spectral modulation detection or SMD) | 6 months post intervention | The spectral modulation detection (SMD) task of spectral resolution will use a 3-interval, 2-alternative forced-choice procedure. The participant will discriminate between flat-spectrum and spectrally-modulated noise presented at 65 dB SPL. We will use a broadband stimulus and assess spectral modulation rates of 0.5 and 1.0 cycle per octave. Threshold will be expressed in modulation depth (in dB) for each modulation rate tested. |
| Secondary | Temporal resolution (sinusoidal amplitude modulation (SAM) detection) | 6 months post intervention | The temporal resolution task includes sinusoidal amplitude modulation (SAM) detection with a 3-interval, 2-alternative forced-choice procedure. The participant will discriminate between noises with a flat temporal envelope and sinusoidal amplitude modulation. We will use a broadband stimulus at 65 dB SPL and assess amplitude modulation rates of 4, 32, and 128 Hz. SAM threshold will be expressed in 20 log m (in dB), with m representing the modulation index (0 to 1). |
| Other | Spectro-temporal modulation (STM) | 6 months post intervention | The spectro-temporal modulation (STM) task will use a 3-interval, 2-alternative forced-choice procedure. STM sensitivity will be measured using a broadband stimulus that has both spectral (1-cycle per octave) and temporal modulation (4- or 32-Hz SAM). We will use a 2-down, 1-up tracking procedure to track 70.7% correct on the psychometric function for all measures. STM threshold will be expressed in spectral modulation depth (in dB) for each of the temporal modulation rates tested. |

4.4. Statistical Design and Power — S1-1_StatisticalDesignPower.pdf

4.5. Subject Participation Duration — 24 months

4.6. Will the study use an FDA-regulated intervention? — ❍ Yes ● No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan — S1-1_DisseminationPlan.pdf

## STATISTICAL ANALYSIS PLAN AND POWER ANALYSES

**Data Management.** Dr. Dietrich (Co-I and biostatistician) will provide support for statistical analyses. All data will be stored in REDCap offering a secure, web-based application.

**Scientific Rigor and Reproducibility.** All data analyses and data sharing will adhere to the NIH's commitment to rigorous and transparent research. This will be accomplished through the analytic approach described here, which replicates our previous analytical approaches used for studies of adult IGCIP (24, 72) and our preliminary study of pediatric IGCIP (4). To achieve transparency, details will be reported that allow other research teams to reproduce the results. Furthermore, raw data will be presented in tables and appendices of our publications and will be made available upon request (within the scope and limits of IRB approved data sharing).

**Statistical Analysis.** *Overall strategy*. Statistical software (SPSS, STATA, R) will be used for the quantitative summarization of data and to test study hypotheses. The reliability of each of the scores from the standardized measures will be assessed and evaluated using Cronbach's alpha statistics. All analyses will be done using *intent-to-treat* principles. Statistical significance tests will maintain Type I error rates of no more than 0.05. Descriptive statistics will summarize and inspect the distributions of study measures for choosing the appropriate modeling procedure for testing hypotheses. A summary of aims, hypotheses, and associated statistical models are shown below in **Table 4**.

***Missing data***. Randomly missing responses to items within assessment tools will be handled via protocols specified by the instrument developers. When there is no protocol, if the participant has completed 75% or more of the items on a particular instrument, the mean score for that instrument will be calculated using available item responses and used in subsequent analyses. In-depth investigations of patterns of missing data will be undertaken to assess if data are missing due to random influences or if there are certain study conditions (e.g. waitlist control) or participant characteristics (e.g., age, hearing function) that are more or less likely to be associated with certain patterns of missing data (i.e. lost to follow-up). We expect that most assessments will not be missing at randomization, thus imputation would not be appropriate.

**TABLE 4**

| HYPOTHESES | MEASURES | STATISTICAL MODELS |
|---|---|---|
| **AIM 1**<br>□ significant positive short-term gain in auditory function for children receiving IGCIP<br>**AIM 2**<br>□ differential growth in auditory function will predict growth in PA, which will predict mediated growth for reading measures<br>**AIM 3:**<br>□ significant positive growth in speech & language; this growth will be predicted by the relative improvement in auditory function from the IGCIP | **AIM 1**<br>□ Spectral, temporal, & spectro-temporal resolution<br>□ Speech recognition<br>□ Subjective questionnaires (auditory & quality of life)<br>**AIM 2**<br>□ PA (Tests & Tasks)<br>□ Reading outcomes (Tests)<br>□ Control for working memory (Tests & Tasks)<br>**AIM 3**<br>□ Language (Tests of expressive, receptive, and narrative)<br>□ Speech production (Tests and Acoustic Analysis) | **AIMS 1-3**<br>□ **Descriptive statistics** of all measures<br>□ **Bootstrapped 95% confidence intervals for all effects**<br>□ **Statistical Control of Potential Confounds:** Covary baseline levels of nonverbal cognition, working memory, and speech recognition<br>□ **Mixed-effects modeling:** Test the differential effect of IGCIP on the trajectories of change in auditory function. 30/group. Minimum detectable effect size = 0.67 (SDs at endpoint); traditional Cohen effect sizes $d$ = 0.2/0.5/0.8 ~ small/medium/large.<br>□ **Cross-lagged panel and path analysis:** Test the mediation effect of key factors on reading outcomes (e.g., phonological awareness on the relationship between auditory function/speech recognition on reading ability and speech production). Minimum detectable path coefficient 0.35 (~12% shared variance)<br>□ **z-test of independent path coefficients.** Test for differences in the size of the path coefficients between the two study groups. |

***Aim 1 and Aim 2: Analysis & hypotheses testing:*** The outcome variables are auditory function, speech recognition, PA, working memory, and reading gains over various time points (**Approach, Table 3**). Descriptive and graphical summaries of trajectories by study group will be conducted initially for detection of outliers and to provide insight into patterns of change. Key statistical tests will involve study group (IGCIP vs. waitlist control) comparisons of the mean slopes resulting from differences in baseline and post-intervention assessments. Tests will be conducted using general linear mixed or multilevel analysis. While randomization ensures equal opportunity for study conditions, it does not ensure equivalence of baseline values. If it is found that group baseline values differ, baseline scores will be included as a covariate in the analysis as will potential confounds such as baseline intellectual level and working memory ability. Within this general multilevel statistical approach, hypothesized differences will be tested by assessing the statistical significance of the main and interaction effects of study group on time-related contrast in baseline and study assessment points in the outcome variable scores. In other words, we expect that the slope of outcome measure scores in the waitlist control group will be nearly '0' while those of immediate IGCIP group will demonstrate a statistically significant positive slope. In addition to statistical significance testing, bootstrapping methods will be used to generate 95% confidence intervals for all sample descriptive (e.g., group means at each time of assessment) and effect estimates (e.g., eta-squared for group effect on linear slope of the outcome scores). Because we expect there to be correlations amongst the multiple outcome

measures, a multivariate approach will provide more unified (systemic) statistical test of the intervention effects.

***Aim 3: Analysis and hypothesis testing:*** The focus of this aim is to explore the complex relationships among changes in the various measures of hearing, speech, and language. As an example of this approach, **Figure 7** displays an example cross-lagged panel analysis which illustrates the structure for statistical analysis of this aim. Via comparisons of the strength of the relationships between the changes in one domain at time 1 with the changes in another domain at time 2, etc., this type of analysis will maximize the information gained from the longitudinal assessment of the multiple domains and inform additional causal hypotheses for subsequent research. Bootstrapped 95% confidence intervals will be generated for each of the path coefficients. For all statistical analyses, we will allow for covariates associated with the child and family including chronological age at assessment, age at CI, age at identification, nonverbal cognition, working memory, gender, and socioeconomic status (10, 15, 119, 120).

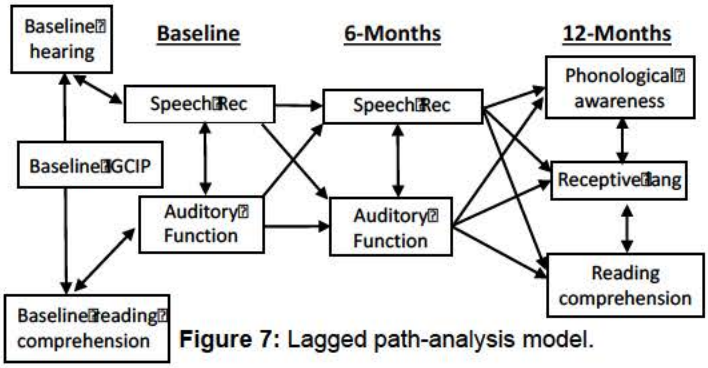



**Figure 7:** Lagged path-analysis model.

***Sample size and power.*** Sample size estimates are based on the desire to detect clinically meaningful effects of the intervention using information from our preliminary studies while maintaining study feasibility. An analysis sample of 30 participants per study group will provide 80% statistical power (two-sided $\alpha$=0.05) for the detection of an intervention effect on the trajectories of the hearing, speech, language, PA and reading as small as 0.32 (Cohen's *d* equivalent=0.67, adjusted for baseline with $\eta^2 \geq 0.2$) and 0.35 (Cohen's *d* equivalent =0.74, unadjusted). Differences of this magnitude are considered to be clinically meaningful. Furthermore, the statistical power estimates are conservative due to the proposed used of mixed-effects analyses approaches that will enable the increased power of treating the repeated assessments as independent values yet appropriately adjusting the standard errors for the correlations among those repeated assessments. The proposed final sample of 60 will enable detection of a path correlation as small as 0.35 (80% power, 2-tailed $\alpha$=0.05). Correlational values of that magnitude or larger were observed in our preliminary work. Detectable differences between the strength of two path coefficients will be 0.4-0.5 (80% power, 2-tailed $\alpha$=0.05) depending on the value of the coefficients and the size each correlation has with other values. The focus of the cross-lagged panel analysis will be on generating effect sizes deepening our understanding of the mechanisms underlying effects of change in hearing on higher-level PA/speech/language downstream. Accounting for 20% attrition, we will enroll 72 patients to achieve a 60-subject sample.

## DISSEMINATION PLAN

We intend to publish data originating from this project in a timely manner in peer-reviewed scientific journals. Data will also be presented at national and international scientific meetings (e.g., American Auditory Society, American Speech-Language-Hearing Association, American Cochlear Implant Alliance, Society for Research in Child Development, Hearing Across the Lifespan). In addition to published papers and conference presentations, unpublished data will be discussed openly with other laboratories and investigators to encourage diversity of analysis and opinion, and to foster collaborative relationships.

We plan to provide summary updates for this project on the PIs' lab websites to help educate clinicians, outside researchers, consumers, as well as current and prospective families on the current project and findings.

The data collected for this project will be saved to our centralized data repository managed by Drs. Gifford and Dawant. We anticipate that the de-identified database will ultimately be available and useful to all clinicians and clinician-scientists for various research-related purposes.

Data analyses and data sharing will be consistent with the NIH's commitment to promoting rigorous and transparent research (see Data Analysis, Approach, Research Strategy). To achieve transparency, details will be reported that allow other research teams to reproduce the results and raw data will be made available in tables and appendices of our publications.

**Delayed Onset Studies**

| Delayed Onset Study# | Study Title | Anticipated Clinical Trial? | Justification |
|---|---|---|---|
| The form does not have any delayed onset studies | | | |

## MULTIPLE PI LEADERSHIP PLAN

### ROLES AND RESPONSIBILITIES

Dr. Gifford and Dr. Camarata will be co-PIs for this project. Given the distinct areas of expertise for the two PIs, the roles and responsibilities for each PI are rather straightforward:

- Dr. Gifford will be responsible for overseeing all research activities relevant to auditory perception.
    - Dr. Gifford will be responsible for overseeing participant recruitment given her role as director of the Cochlear Implant Program in the Department of Hearing and Speech Sciences at the Vanderbilt Bill Wilkerson Center.
- Dr. Camarata will be responsible for overseeing all research activities relevant to speech, language, and literacy.
    - Dr. Camarata will be responsible for the mentorship of the SLP graduate research assistant.
- Drs. Gifford and Camarata will share mentorship of the PhD student who will be working across both areas of specialty with outcomes for pediatric CI recipients as his/her research focus.

Further, Drs. Gifford and Camarata will be provided with monthly budget reports for the project. Both will review the fiscal data and will briefly discuss at the monthly project meeting (discussed below).

### COMMUNICATION PLAN

Dr. Gifford and Dr. Camarata [redacted] have been collaborating on the preliminary studies and project development since 2013. Thus there is a history of across-laboratory communication which will be continued and strengthened throughout the duration of this project. We will hold monthly project meetings during which all study personnel housed in each laboratory will discuss project progress, present preliminary data for group discussion, identify concerns regarding participant recruitment progress and data collection, and map project goals for the following month, quarter, and year.

### SCIENTIFIC DIRECTION

The direction of the research is spelled out in detail in our Research Plan. Deviations from the defined Research Plan will be made only if both PIs agree.

### RESOLVING CONFLICTS

Because we will be following a well-defined research plan and a history of collaboration, we anticipate few, if any conflicts. However, should a conflict arise, disagreement will be referred to an arbitration committee including two independent senior faculty from Vanderbilt University Medical Center and one independent senior faculty member from an outside institution, the latter of whom both PIs will be required to mutually agree upon. The members of the arbitration committee will not be involved in either PIs' lines of research.

### PUBLICATION AND INTELLECTUAL PROPERTY POLICIES

Publications arising from this project will include both Dr. Gifford and Dr. Camarata as authors. For publications focusing on auditory outcomes, Dr. Gifford will serve as senior author. For publications focusing on speech, language, and/literacy outcomes, Dr. Camarata will serve as senior author.

### CHANGE IN PI LOCATION

If one of the PIs moves to a new institution, we will transfer the relevant portion of the grant to the new institution. In the event that a PI cannot carry out his/her duties at the new institution, a new PI will be recruited as a replacement at the home institution, Vanderbilt University Medical Center.

### BUDGET ALLOCATION

Please see budget justification for allocation of resources.

## REFERENCES


1. Gifford H, Olund AP, Dejong M. Improving Speech Perception in Noise for Children with Cochlear Implants. 2012;632(2011):623–32.
2. Gifford RH, Dorman MF, Skarzynski H, Lorens A, Polak M, Driscoll CLW, et al. Cochlear implantation with hearing preservation yields significant benefit for speech recognition in complex listening environments. Ear Hear. 2013;34(4).
3. Uhler K, Warner-Czyz A, Gifford R, Group PW. Pediatric Minimum Speech Test Battery. J Am Acad Audiol. 2017;28(3):232–47.
4. Noble JH, Hedley-Williams AJ, Sunderhaus L, Dawant BM, Labadie RF, Camarata SM, et al. Initial Results With Image-guided Cochlear Implant Programming in Children. Otol Neurotol. 2016;37(2):e63–9.
5. Nittrouer, S., Caldwell, A., Holloman C. Effectively predicting language and literacy in children with cochlear implants. Int Joural Pediatr Otorhinolaryngol. 2012;76(8):1148–58.
6. Ruffin C V., Kronenberger WG, Colson BG, Henning SC, Pisoni DB. Long-term speech and language outcomes in prelingually deaf children, adolescents and young adults who received cochlear implants in childhood. Audiol Neurotol. 2013;18(5):289–96.
7. Mayer, C., Trezek BJ. Literacy Outcomes in Deaf Students with Cochlear Implants: Current State of the Knowledge. J Deaf Stud Deaf Educ. 2017;23(1):1–16.
8. Nittrouer S, Caldwell-Tarr A. Language and literacy skills in children with cochlear implants: past and present findings. In: Pediatric Cochlear Implantation. 2016. p. 177–97.
9. Leigh, J. R., Dettman, S. J., Dowell RC. Evidence-based guidelines for recommending cochlear implantation for young children: Audiological criteria and optimizing age at implantation. Int J Audiol. 2016;55 Suppl 2:S9–S18.
10. Tobey E a, Thal D, Niparko JK, Eisenberg LS, Quittner AL, Wang N-Y. Influence of implantation age on school-age language performance in pediatric cochlear implant users. Int J Audiol [Internet]. 2013;52(4):219–29. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3742378&tool=pmcentrez&rendertype=abstract
11. Niparko, J. K., Tobey, E. A., Thal, D. J., Eisenberg, L. S., Wang, N. Y., Quittner, A. L., Fink, N. E. CdIT. Spoken Language Development in Children Following Cochlear Implantation. J Am Med Assoc. 2010;303(15):1498–506.
12. Sharma A, Campbell J, Cardon G. Developmental and cross-modal plasticity in deafness: Evidence from the P1 and N1 event related potentials in cochlear implanted children. Int J Psychophysiol [Internet]. 2015;95(2):135–44. Available from: http://dx.doi.org/10.1016/j.ijpsycho.2014.04.007
13. Langereis, M., Vermeulen A. School performance and wellbeing of children with CI in different communicative-educational environments. Int Joural Pediatr Otorhinolaryngol. 2015;79(6):834–9.
14. Leigh JR, Dettman SJ, Dowell RC. Evidence-based guidelines for recommending cochlear implantation for young children: Audiological criteria and optimizing age at implantation. Int J Audiol [Internet]. 2016;55 Suppl 2(sup2):S9–18. Available from: http://www.tandfonline.com/doi/full/10.3109/14992027.2016.1146415%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/27142630
15. Niparko JK, Tobey EA, Thal DJ, Eisenberg LS, Wang N-Y, Quittner AL, et al. Spoken Language Development in Children Following Cochlear Implantation. J Am Med Assoc. 2010;303(15):1498–506.
16. Sharma A, Gilley PM, Dorman MF, Baldwin R. Deprivation-induced cortical reorganization in children with cochlear implants. Int J Audiol [Internet]. 2007;46(9):494–9. Available from: http://www.tandfonline.com/doi/full/10.1080/14992020701524836
17. Dettman SJ, Dowell RC, Choo D, Arnott W, Abrahams Y, Davis A, et al. Long-term Communication Outcomes for Children Receiving Cochlear Implants Younger Than 12 Months. Otol Neurotol [Internet]. 2016;37(2):e82–95. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00129492-201602000-00027
18. Newman, R., Chatterjee M. Toddlers' recognition of noise-vocoded speech. J Acoust Soc Am. 2013;133(1):483–494.

19. Nittrouer S, Lowenstein JH. Weighting of Acoustic Cues to a Manner Distinction by Children With and Without Hearing Loss. J Speech, Lang Hear Res. 2015;24(2):1077–92.
20. Gifford, R. H., Noble, J. H., Camarata, S. M., Sunderhaus, L. W., Dwyer, R. T., Dawant, B. M., Dietrich, M., Labadie RF. The relationship between spectral modulation detection and speech recognition: adult versus pediatric cochlear implant recipients. Trends Hear. 2018;22(1–15).
21. Nittrouer S, Caldwell A, Holloman C. Measuring what matters: Effectively predicting language and literacy in children with cochlear implants. Int J Pediatr Otorhinolaryngol [Internet]. 2012;76(8):1148–58. Available from: http://dx.doi.org/10.1016/j.ijporl.2012.04.024
22. Tinnemore, A. R., Zion, D. J., Kulkarni, A. M., Chatterjee M. Children's Recognition of Emotional Prosody in Spectrally Degraded Speech Is Predicted by Their Age and Cognitive Status. Ear Hear. 2018;2018 Jan 1.
23. Nittrouer S, Lowenstein JH, Holloman C. Early predictors of phonological and morphosyntactic skills in second graders with cochlear implants. Res Dev Disabil. 2016;55:143–60.
24. Noble JH, Gifford RH, Hedley-Williams AJ, Dawant BM, Labadie RF. Clinical evaluation of an image-guided cochlear implant programming strategy. Audiol Neurotol. 2014;19(6).
25. Noble JH, Gifford RH, Labadie RF, Dawant BM. Statistical shape model segmentation and frequency mapping of cochlear implant stimulation targets in CT. Med Image Comput Comput Assist Interv. 2012;15.
26. Noble JH, Labadie RF, Gifford RH, Dawant BM. Image-Guidance enables new methods for customizing cochlear implant stimulation strategies. IEEE Trans Neural Syst Rehabil Eng. 2013;21(5).
27. Nicholas JG, Geers AE. Will they catch up? The role of age at cochlear implantation in the spoken language development of children with severe to profound hearing loss. J Speech Lang Hear Res [Internet]. 2007;50(4):1048–62. Available from: http://jslhr.pubs.asha.org/article.aspx?doi=10.1044/1092-4388(2007/073)
28. Geers AE, Strube MJ, Tobey EA, Pisoni DB, Moog JS. Epilogue: Factors Contributing to Long-Term Outcomes of Cochlear Implantation in Early Childhood. Ear Hear [Internet]. 2011;32:84S–92S. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003446-201102001-00010
29. Geers AE, Tobey EA, Moog J, Brenner C. Long-term outcomes of cochlear implantation in the preschool years: From elementary grades to high school. Int J Audiol. 2008;47(S2):S21-30.
30. Hayes H, Geers AE, Treiman R, Moog JS. Receptive vocabulary development in deaf children with cochlear implants: achievement in an intensive auditory-oral educational setting. Ear Hear. 2009;30(1):128–35.
31. Holt RF, Beer J, Kronenberger WG, Pisoni DB, Lalonde K. Contribution of family environment to pediatric cochlear implant users' speech and language outcomes: some preliminary findings. J Speech Lang Hear Res. 2012;55(3):848–64.
32. Bouton, S., Serniclaes, W., Bertoncini, J., Colé P. Perception of speech features by French-speaking children with cochlear implants. J Speech, Lang Hear Res. 2012;55(1):139–53.
33. Peng SC, Tomblin JB, Cheung H, Lin YS, Wang LS. Perception and production of mandarin tones in prelingually deaf children with cochlear implants. Ear Hear. 2004;25(3):251–64.
34. Lee KY, van Hasselt CA, Chiu SN, Cheung DM. Cantonese tone perception ability of cochlear implant children in comparison with normal-hearing children. Int J Pediatr Otorhinolaryngol. 2002;63(2):137–47.
35. Yeung HH, Werker JF. Learning words' sounds before learning how words sound: 9-Month-olds use distinct objects as cues to categorize speech information. Cognition [Internet]. 2009;113(2):234–43. Available from: http://dx.doi.org/10.1016/j.cognition.2009.08.010
36. Olszewski C, Gfeller K, Froman R, Stordahl J, Tomblin B. Familiar melody recognition by children and adults using cochlear implants and normal hearing children. Cochlear Implants Int. 2005;6(3):123–40.
37. Jung KH, Won JH, Drennan WR, Jameyson E, Miyasaki G, Norton SJ, et al. Psychoacoustic performance and music and speech perception in prelingually deafened children with cochlear implants. Audiol Neurotol. 2012;17(3):189–97.
38. Rosen S. Temporal information in speech: acoustic, auditory, and linguistic aspects. Philos Trans Biol Sci. 1992;336(1278):367–73.
39. van Tasell DJ, Soli SD, Kirby VM, Widin GP. Speech waveform envelope cues for consonant recognition. J Acoust Soc Am. 1987;82(4):1152–61.
40. van Tasell DJ, Greenfield DG, Logemann JJ, Nelson DA. Temporal cues for consonant recognition:

training, talker generalization, and use in evaluation of cochlear implants. J Acoust Soc Am. 1992;92:1247–57.
41. Shannon R V., Zeng FG, Kamath V, Wygonski J, Ekelid M. Speech Recognition with Primarily Temporal Cues. Science (80- ). 1995;270:303–4.
42. Hong, R. S., Rubinstein JT. High-rate conditioning pulse trains in cochlear implants: dynamic range measures with sinusoidal stimuli. J Acoust Soc Am. 2003;114:3327–3342.
43. Litvak, L. M., Smith, Z. M., Delgutte, B., Eddington DK. Desynchronization of electrically evoked auditory nerve activity by highfrequency pulse trains of long duration. J Acoust Soc Am. 2003;114:2066–78.
44. Loizou, P. C., Poroy O. Minimum spectral contrast needed for vowel identification by normal hearing and cochlear implant listeners. J Acoust Soc Am. 2001;110:1619–27.
45. Drennan WR, Won JH, Nie K, Jameyson E, Rubinstein JT. Sensitivity of psychophysical measures to signal processor modifications in cochlear implant users. Hear Res. 2010;262(2–2):1–8.
46. Holder, J. T., Kessler, D., Gifford, R. H., Noble, J. H., Labadie RF. Prevalence of extracochlear electrodes: CT scans, cochlear implant maps, and operative reports. Otol Neurotol. 2018;epub ahead.
47. Bierer JA, Litvak L. Channel Interaction Through Cochlear Implant Programming May Improve Speech Perception: Current Focusing and Channel Deactivation. Trends Hear. 2016;20:1–12.
48. Vickers D, Degun A, Canas A, Stainsby T, Vanpoucke F. Deactivating Cochlear Implant Electrodes Based on Pitch Information for Users of the ACE Strategy. Adv Exp Med Biol. 2016;894:115–23.
49. Zhou N. Deactivating stimulation sites based on low-rate thresholds improves spectral ripple and speech reception thresholds in cochlear implant users. J Acoust Soc Am. 2017;141(3):EL243.
50. Debruyne JA, Francart T, Janssen AM, Douma K, Brokx JP. Fitting prelingually deafened adult cochlear implant users based on electrode discrimination performance. Int J Audiol. 2017;56(3):174–85.
51. Mens LH, Berenstein CK. Speech perception with mono- and quadrupolar electrode configurations: a crossover study. Otol Neurotol. 2005;26(5):957–64.
52. Srinivasan AG, Landsberger DM, Shannon R V. Current Focusing Sharpens Local Peaks of Excitation in Cochlear Implant Stimulation. Hear Res [Internet]. 2010;270(1–2):89–100. Available from: http://tia.sagepub.com/cgi/doi/10.1177/2331216516653389
53. Frijns JH, Dekker DM, Briaire JJ. Neural excitation patterns induced by phased-array stimulation in the implanted human cochlea. Acta Otolaryngol. 2011;131(4):362–70.
54. Bierer JA, Faulkner KF, Tremblay KL. Identifying cochlear implant channels with poor electrode-neuron interface: electrically-evoked auditory brainstem responses measured with the partial tripolar configuration. Ear Hear. 2011;32(4):436–44.
55. Litvak LM, Spahr AJ, Emadi G. Loudness growth observed under partially tripolar stimulation: model and data from cochlear implant listeners. J Acoust Soc Am [Internet]. 2007;122(2):967–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17672645
56. Padilla M, Landsberger DM. Reduction in spread of excitation from current focusing at multiple cochlear locations in cochlear implant users. Hear Res. 2016;333:98–107.
57. Landsberger DM, Srinivasan AG. Virtual channel discrimination is improved by current focusing in cochlear implant recipients. Hear Res. 2009;254(1–2):34–41.
58. Arenberg JG, Parkinson WS, Litvak L, Chen C, Kreft HA, Oxenham AJ. A Dynamically Focusing Cochlear Implant Strategy Can Improve Vowel Identification in Noise. Ear Hear. 2018;2018 March:epub ahead of print.
59. Won JH, Drennan WR, Nie K, Jameyson EM, Rubinstein JT. Acoustic temporal modulation detection and speech perception in cochlear implant listeners. J Acoust Soc Am [Internet]. 2011;130(1):376–88. Available from: http://asa.scitation.org/doi/10.1121/1.3592521
60. Saoji AA, Litvak L, Spahr AJ, Eddins DA. Spectral modulation detection and vowel and consonant identifications in cochlear implant listeners. J Acoust Soc Am [Internet]. 2009;126(3):955–8. Available from: isi:000269833600009
61. Litvak LM, Spahr AJ, Saoji AA, Fridman GY. Relationship between perception of spectral ripple and speech recognition in cochlear implant and vocoder listeners. J Acoust Soc Am. 2007;122(2):982–91.
62. Drennan WR, Won JH, Nie K, Jameyson E, Rubinstein JT. Sensitivity of psychophysical measures to signal processor modifications in cochlear implant users. Hear Res. 2010;262(1–2):1–8.
63. Zhang T, Spahr AJ, Dorman MF, Saoji A. Relationship Between Auditory Function of Nonimplanted Ears and Bimodal Benefit. Ear Hear [Internet]. 2013;34(2):133–41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23075632

64. Gifford RH, Hedley-Williams A, Spahr AJ. Clinical assessment of spectral modulation detection for adult cochlear implant recipients: A non-language based measure of performance outcomes. Int J Audiol. 2014;53(3).
65. Altmann CF, Gaese BH. Representation of frequency-modulated sounds in the human brain. Hear Res [Internet]. 2014;307:74–85. Available from: http://dx.doi.org/10.1016/j.heares.2013.07.018
66. Drennan WR, Anderson ES, Won JH, Rubinstein JT. Validation of a clinical assessment of spectral-ripple resolution for cochlear implant users. Ear Hear [Internet]. 2014;35(3):e92-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24552679
67. Henry BA, Turner CW, Behrens A. Spectral peak resolution and speech recognition in quiet: normal hearing, hearing impaired, and cochlear implant listeners. J Acoust Soc Am [Internet]. 2005;118(2):1111–21. Available from: http://scitation.aip.org/content/asa/journal/jasa/118/2/10.1121/1.1944567
68. Henry BA, Turner CW. The resolution of complex spectral patterns by cochlear implant and normal-hearing listeners. J Acoust Soc Am. 2003;113(5):2861–2873.
69. Won JH, Drennan WR, Rubinstein JT. Spectral-ripple resolution correlates with speech reception in noise in cochlear implant users. JARO - J Assoc Res Otolaryngol. 2007;8(3):384–92.
70. Drennan WR, Won JH, Timme AO, Rubinstein JT. Non-linguistic outcome measures in adult cochlear implant users over the first year of implantation. Vol. 37. 2016. 354-364 p.
71. Labadie RF, Noble H, Hedley-Williams J, Sunderhaus ZW, Dawant M, Gifford ZH. Results of Postoperative, CT-based, Electrode Deactivation on Hearing in Prelingually Deafened Adult Cochlear Implant Recipients. Otol Neurotol. 2016;37:137–45.
72. Landsberger DM, Padilla M, Martinez AS, Eisenberg LS. Spectral-Temporal Modulated Ripple Discrimination by Children With Cochlear Implants. Ear Hear. 2017;epub ahead.
73. Horn DL, Dudley DJ, Dedhia K, Nie K, Drennan WR, Won JH, et al. Effects of age and hearing mechanism on spectral resolution in normal hearing and cochlear-implanted listeners. J Acoust Soc Am. 2017;613–623.
74. DiNino M, Arenberg JG. Age-Related Performance on Vowel Identification and the Spectral-temporally Modulated Ripple Test in Children With Normal Hearing and With Cochlear Implants. Trends Hear. 2018;22:1–20.
75. Nittrouer S, Caldwell-Tarr A, Lowenstein JH. Working memory in children with cochlear implants: problems are in storage, not processing. Int J Pediatr Otorhinolaryngol. 2013;77:1886–98.
76. Nittrouer S, Caldwell-Tarr A, Low KE, Lowenstein JH. Verbal Working Memory in Children With Cochlear Implants. J Speech, Lang Hear Res. 2017;60:3342–64.
77. Camarata, S., Werfel, K., Davis, T., Hornsby, B. & Bess F. Language Abilities, Phonological Awareness, Reading Skills, and Subjective Fatigue in School-Age Children with Mild-to-Moderate Hearing Loss. Except Child. 2018;epub ahead.
78. Pisoni DB, Kronenberger WG, Roman AS, Geers AE. Measures of digit span and verbal rehearsal speed in deaf children after more than 10 years of cochlear implantation. Ear Hear. 2011;32:60S–74S.
79. McCreery RW, Spratford M, Kirby B, Brennan M. Individual differences in language and working memory affect children's speech recognition in noise. Int J Audiol. 2017;56:306–15.
80. Ingvalson EM, Young NM, Wong PC. Auditory-cognitive training improves language performance in prelingually deafened cochlear implant recipients. Int J Pediatr Otorhinolaryngol. 2014;78(10):1624–31.
81. Harris MS, Pisoni DB, Kronenberger WG, Gao S, Caffrey HM, Miyamoto RT. Developmental trajectories of forward and backward digit spans in deaf children with cochlear implants. Cochlear Implants Int. 2011;12 Suppl 1:S84–S88.
82. Cooper R, Rosenstein J. Language acquisition of deaf children. Volta Rev. 1966;68(1):58–67.
83. Fry DB, Whetnall E. The auditory approach in the training of deaf children. Lancet. 1954;263(6812):583–7.
84. Hampleman RS. Comparison of listening and reading comprehension ability of fourth and sixth grade pupils. Elem English. 1958;35(1):49–53.
85. Harris, M., Terlektsi, E., & Kyle FE. Literacy outcomes for primary school children who are deaf and hard of hearing: A cohort comparison study. J Speech, Lang Hear Res. 2017;60(3):701–11.
86. Meinzen-Derr, J., Sheldon, R., Grether, S., Altaye, M., Smith, L., Choo, D. I., Wiley S. Underperformance in Young Children Who Are Deaf or Hard-of-Hearing: Are the Expectations Too Low? J Dev Behav Pediatr. 2018;39(2):116–25.

87. Johnson C, Goswami U. Phonological awareness, vocabulary and reading in deaf children with cochlear implants. J Speech Lang Hear Res. 2010;53:237–61.
88. Nittrouer S, Sansom E, Low K, Rice C, Caldwell-Tarr A. Language structures used by kindergartners with cochlear implants: relationship to phonological awareness, lexical knowledge and hearing loss. Ear Hear. 2014;35(5):506–18.
89. Deeb D, Gao X, Jiang H, Arbab AS, Dulchavsky SA, Gautam SC. Growth inhibitory and apoptosis-inducing effects of xanthohumol, a prenylated chalone present in hops, in human prostate cancer cells. Anticancer Res. 2010;30(9):3333–9.
90. Bailey, P. J., Snowling MJ. Auditory processing and the development of language and literacy. Br Med Bull. 2002;63:135–46.
91. Nittrouer, S., Lowenstein JH. Learning to perceptually organize speech signals in native fashion. J Acoust Soc Am. 2010;127(3):1624–35.
92. White-Schwoch, T., Carr, K. W., Thompson, E. C., Anderson, S., Nicol, T., Bradlow, A. R., Zecker, S.G. & Kraus N. Auditory processing in noise: A preschool biomarker for literacy. PLoS Biol. 2015;13(7):e1002196.
93. Carroll, J. M., & Snowling MJ. The effects of global similarity between stimuli on children's judgments of rime and alliteration. Appl Psycholinguist. 2001;22:327–42.
94. Metsala, J. L., & Walley AC. Spoken vocabulary growth and the segmental restructuring of lexical representations: precursors to phonemic awareness and early reading ability. In: Ehri JLM& LC, editor. Word recognition in beginning literacy. Hillsdale, NJ: Erlbaum; 1998. p. 89–120.
95. Venturaa, P., Kolinsky, R., Fernandesa, S., Queridoa, L., Morais J. Lexical restructuring in the absence of literacy. Cognition. 2007;105(2):334–61.
96. Carroll, J. M., Snowling, M. J., Hulme, C., Stevenson J. The development of phonological awareness in preschool children. Dev Psychol. 2003;39:913–23.
97. Storkel HL. Learning new words: Phonotactic probability in language development. J Speech, Lang Hear Res. 2001;44(6):1321–37.
98. Nittrouer, S., Caldwell, A., Lowenstein, J. H., Tarr, E., Holloman C. Emergent literacy in kindergartners with cochlear implants. Ear Hear. 2012;33(6):683–97.
99. Klein, K. E., Walker, E. A., Kirby, B., & McCreery RW. Vocabulary Facilitates Speech Perception in Children With Hearing Aids. J Speech, Lang Hear Res. 2017;60(8):2281–96.
100. Nittrouer, S., Studdert-Kennedy, M., & McGowan RS. The emergence of phonetic segments: Evidence from the spectral structure of fricative-vowel syllables spoken by children and adults. J Speech, Lang Hear Res. 1989;32(1):120–32.
101. Han MK, Storkel HL, Lee J, Yoshinaga-Itano C. The influence of word characteristics on the vocabulary of children with cochlear implants. J Deaf Stud Deaf Educ. 2015;20(3):242–51.
102. Baer T, Moore BCJ, Gatehouse S. Spectral contrast enhancement of speech in noise for listeners with sensorineural hearing impairment: effects on intelligibility, quality, and response times. J Rehabil Res Dev. 1993;30(1):49–72.
103. Nittrouer, S., Tarr, E., Wucinich, T., Moberly, A. C., Lowenstein JH. Measuring the effects of spectral smearing and enhancement on speech recognition in noise for adults and children. J Acoust Soc Am [Internet]. 2015;137(4):2004–14. Available from: http://asa.scitation.org/doi/10.1121/1.4916203
104. Wanna GB, Balachandran R, Majdani O, Mitchell J, Labadie RF. Percutaneous access to the petrous apex in vitro using customized micro-stereotactic frames based on image-guided surgical technology. Acta Otolaryngol. 2009;25:1–6.
105. Schuman TA, Noble JH, Wright CG, Wanna GB, Dawant BM, Labadie RF. Anatomic verification of a novel method for precise intrascalar localization of cochlear implant electrodes in adult temporal bones using clinically available computed tomography. Laryngoscope. 2010;120(11):2277–83.
106. Peterson GE, Lehiste I. Revised CNC lists for auditory tests. J Speech Hear Disord. 1962;27:62–70.
107. Spahr AJ, Dorman MF, Litvak LM, Cook SJ, Loiselle LM, Dejong MD, et al. Development and validation of the pediatric AzBio sentence lists. Ear Hear. 2014;35(4).
108. Etymotic R. BKB-SIN TEST. 2005.
109. Holder JT, Sheffield SW, Gifford RH. Speech understanding in children with normal hearing: Sound field normative data for babybio, BKB-SIN, and QuickSIN. Otol Neurotol. 2016;37(2).
110. Fu Q-J. Temporal processing and speech recognition in cochlear implant users. Neuroreport [Internet]. 2002;13(13):1635–9. Available from:

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2704892&tool=pmcentrez&rendertype=abstract
111. Carrow-Woolfolk E. Test of Auditory Comprehension of Language (TACL3). Austin, Texas; 1999.
112. Goldman R, Fristoe M. Goldman-Fristoe Test of Articulation, 2nd edition (GFTA-2). Bloomington, MN; 2000.
113. Casserly ED, Pisoni DB. Nonword repetition as a predictor of long-term speech and language skills in children with cochlear implants. Otol Neurotol. 2013;34(3):460–70.
114. Nittrouer, S., Caldwell-Tarr, A., Sansom, E., Twersky, J., & Lowenstein JH. Nonword repetition in children with cochlear implants: A potential clinical marker of poor language acquisition. Am J speech-language Pathol. 2014;23(4):679–95.
115. Wiseman, K. B., Warner-Czyz A. Inconsistent device use in pediatric cochlear implant users: Prevalence and risk factors. Cochlear Implants Int. 2018;19:131–41.
116. Busch, T., Vanpoucke, F., van Wieringen A. Auditory environment across the life span of cochlear implant users: insights from data logging. J Speech, Lang Hear Res. 2017;60:1362–77.
117. Moog JS, Geers AE. Early educational placement and later language outcomes for children with cochlear implants. Otol Neurotol. 2010;31(8):1315–9.
118. Tobey EA, Geers AE, Brenner C, Altuna D, Gabbert G. Factors Associated with Development of Speech Production Skills in Children Implanted by Age Five. Ear Hear. 2003;24:36S–45S.
119. Davidson LS, Geers AE, Brenner C. Cochlear implant characteristics and speech perception skills of adolescents with long-term device use. Otol Neurotol. 2010;31(8):1310–4.
120. Skinner MW, Holden LK, Holden TA, Demorest ME. Comparison of Two Methods for Selecting Minimum Stimulation Levels Used in Programming the Nucleus 22 Cochlear Implant. J Speech, Lang Hear Res. 1999;42:814–28.
121. Walkowiak A, Lorens A, Kostek B, Skarzynski H, Polak M. ESRT, ART, and MCL Correlations in Experienced Paediatric Cochlear Implant Users. Cochlear Implants Int [Internet]. 2010;11(sup1):482–4. Available from: http://www.tandfonline.com/doi/full/10.1179/146701010X12671177204741
122. Wolfe J, Gilbert M, Schafer E, Litvak LM, Spahr AJ, Saoji A, et al. Optimizations for the Electrically-Evoked Stapedial Reflex Threshold Measurement in Cochlear Implant Recipients. Ear Hear. 2016;1–7.
123. de Andrade KCL, Muniz LF, Menezes PL, Neto SDSC, Carnaúba ATL, Leal MC. The Value of Electrically Evoked Stapedius Reflex in Determining the Maximum Comfort Level of a Cochlear Implant. J Am Acad Audiol. 2018;29(4):292–9.
124. Scollie S, Seewald R, Cornelisse L, Moodie S, Bagatto M, Laurnagaray D, et al. The Desired Sensation Level multistage input/output algorithm. Trends Amplif. 2005;9(4):159–97.
125. Friesen LM, Shannon R V., Baskent D, Wang X. Speech recognition in noise as a function of the number of spectral channels: comparison of acoustic hearing and cochlear implants. J Acoust Soc Am [Internet]. 2001;110(2):1150–63. Available from: http://link.aip.org/link/JASMAN/v110/i2/p1150/s1&Agg=doi
126. Shannon R V., Cruz RJ, Galvin JJ. Effect of stimulation rate on cochlear implant users' phoneme, word and sentence recognition in quiet and in noise. Audiol Neurotol. 2011;16(2):113–23.
127. Noble, J. H., Gifford, R. H., Hedley-Williams, A. J., Dawant, B. M., Labadie RF. Clinical evaluation of an imageguided cochlear implant programming strategy. Audiol Neurootol. 2014;19(6):400–11.
128. Saoji AA, Eddins DA. Spectral modulation masking patterns reveal tuning to spectral envelope frequency. J Acoust Soc Am [Internet]. 2007;122(2):1004–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17672648
129. Viemeister NF. Temporal modulation transfer functions based upon modulation thresholds. J Acoust Soc Am. 1979;66(5):1364–80.
130. Houtgast T, Steeneken HJM. A review of the MTF concept in room acoustics and its use for estimating speech intelligibility in auditoria. J Acoust Soc Am [Internet]. 1985;77(3):1069–77. Available from: http://asa.scitation.org/doi/10.1121/1.392224
131. Bernstein, J. G., Danielsson, H., Hällgren, M., Stenfelt, S., Rönnberg, J. LT. Spectrotemporal Modulation Sensitivity as a Predictor of Speech-Reception Performance in Noise With Hearing Aids. Trends Hear. 2016;20:1–20.
132. Levitt H. Transformed up-down methods in psychoacoustics. J Acoust Soc Am. 1971;49(2):467–77.
133. Metsala, J. L., Stavrinos, D., & Walley AC. Children's spoken word recognition and contributions to phonological awareness and nonword repetition: A 1-year follow-up. Appl Psycholinguist.

2009;30(1):101–21.
134. Nilsson M, Soli SD, Sullivan JA. Development of the Hearing in Noise Test for the measurement of speech reception thresholds in quiet and in noise. J Acoust Soc Am. 1994;95(2):1085–99.
135. Lebo CP, Smith MFW, Mosher ER, Jelonek SJ, Schwind DR, Decker KE, et al. Restaurant Noise, Hearing Loss, and Hearing Aids. West J Med. 1994;161(1):45–9.
136. Farber GS, Wang LM. Analyses of crowd-sourced sound levels of restaurants and bars in New York City. Proc Mtgs Acoust. 2017;31:1–15.
137. Crukley J, Scollie S, Parsa V. An Exploration of Non-Quiet Listening at School. J Educ Audiol. 2011;17:23–35.
138. Pearsons KS, Bennett RL, Fidell S. Speech levels in various noise environments. Washington, DC; 1977.
139. Lee, Y., Yim, D., & Sim H. Phonological processing skills and its relevance to receptive vocabulary development in children with early cochlear implantation. Int Joural Pediatr Otorhinolaryngol. 2012;76(12):1755–60.
140. Thornton, A. R., Raffin MJ. Speech-discrimination scores modeled as a binomial variable. J Speech Hear Res. 1978;21(3):507–18.
141. Meinzen-Derr J, Wiley S, Creighton J, Choo D. Auditory Skills Checklist: clinical tool for monitoring functional auditory skill development in young children with cochlear implants. Ann Otol Rhinol Laryngol. 2007;116(11):812–8.
142. Ching TYC, Hill M. The Parents' Evaluation of Aural/Oral Performance of Children (PEACH) Scale: Normative Data. J Am Acad Audiol. 2007;18:220–35.
143. Varni J, Seid M, Kurtin PS. PedsQL 4.0: Reliability and Validity of the Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales in Healthy and Patient Populations. Med Care. 2001;39(8):800–12.
144. Brownell R. Receptive One-Word Picture Vocabulary Tests, Fourth Edition (ROWPVT-4). Bloomington, MN; 2010.
145. Dunn LM, Dunn DM. Peabody Picture Vocabulary Test, Fourth Edition (PPVT$^{TM}$-4). Bloomington, MN; 2007.
146. Carrow-Woolfolk E. TACL-4: Test for Auditory Comprehension of Language–Fourth Edition. Austin, Texas; 2014.
147. Semel E, Wiig EH, Secord WA. Clinical Evaluation of Language Fundamentals® - Fourth Edition (CELF® - 4). Bloomington, MN; 2003.
148. Brownell R. Expressive One-Word Picture Vocabulary Tests, Fourth Edition (EOWPVT-4). Bloomington, MN; 2010.
149. Dawson J, Stout C. SPELT-3: The Structured Photographic Expressive Language Test -Third Edition. Greenville, SC; 2003.
150. Goldman R, Fristoe M. Goldman-Fristoe Test of Articulation 3: (GFTA-3). Bloomington, MN; 2015.
151. Glasgow C, Cowley J. Renfrew Bus Story test - North American Edition. Centreville, DE;
152. Berisha V, Liss J, Wisler A. Aural Analytics. Tempe, AZ: Aural Analytics, LLC; 2015.
153. Jiao Y, Berisha V, Liss J. Interpretable phonological features for clinical applications. In: IEEE International Conference on Acoustics, Speech, and Signal Processing. New Orleans, LA; 2017.
154. Roid GH, Miller LJ. Leiter International Performance Scale, Third Edition. 2013.
155. Schrank FA, McGrew KS, Mather N. Woodcock-Johnson IV. Riverside, IL: Rolling Meadows; 2014.
156. Melby-Lervag M, Hulme C. Serial and free recall in children can be improved by training: evidence for the importance of phonological and semantic representations in immediate memory tasks. Psychol Sci. 2010;21:1694–700.
157. Nittrouer S, Miller ME. The development of phonemic coding strategies for serial recall. Appl Psycholinguist. 1999;20:563–88.
158. Gillon GT. Phonological Awareness. 2nd editio. New York, NY: Guilford Press; 2017.
159. Wagner R, Torgesen J, Rashotte C, Pearson NA. Comprehensive Test of Phonological Processing, Second Edition (CTOPP-2). Bloomington, MN; 2013.
160. Martin NA, Brownell R. Test of Auditory Processing Skills, third edition (TAPS-3). Austin, Texas; 2005.
161. Ching TY, Cupples L. Phonological Awareness at 5 years of age in Children who use Hearing Aids or Cochlear Implants. Perspect Hear Hear Disord Child. 2015;25(2):48–59.
162. Fuchs D, Hendricks E, Walsh ME, Fuchs LS, Gilbert JK, Tracy WZ, et al. Evaluating a Multidimensional Reading Comprehension Program and Reconsidering the Lowly Reputation of Tests of Near-Transfer.

Learn Disabil Res Pract. 2018;33(1):11–23.
163. Woodcock RW. Woodcock Reading Mastery Tests, Third Edition (WRMT™-III). Bloomington, MN; 2011.
164. Bryant BR, Wiederholt JL. GORT-5: Gray Oral Reading Tests−Fifth Edition. Bloomington, MN; 2011.

VANDERBILT UNIVERSITY MEDICAL CENTER

OFFICE OF SPONSORED PROGRAMS

Main [redacted] Fax (615-343-2447)

# Letter of Intent to Establish a Consortium

**Title of Application:** Image-Guided Cochlear Implant Programming: Pediatric Speech, Language, and Literacy

**Applicant/Prime Institution:** Vanderbilt University Medical Center

**Principal Investigator:** Renee Gifford/Stephen Camarata

**Cooperating/Subrecipient Institution:** Vanderbilt University

**Co-Investigator:** Jack Noble

**Costs requested by Cooperating Institution**

**Proposed Effective Date:** 04/01/2019

| | | | |
|---|---|---|---|
| First Budget Year: | 04/01/2019-03/31/2020 | Project Period: | 04/01/2019-03/31/2024 |
| Direct Costs: | [redacted] | Direct Costs: | [redacted] |
| F & A Costs: | | F & A Costs: | |
| **Total:** | | **Total:** | |

Completion of this form signifies that this proposal has been reviewed, approved, and certified for accuracy by the appropriate institutional official. The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the awarding agency's policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy. The amounts shown above appear in the application; however, Vanderbilt University Medical Center reserves the right to negotiate terms and conditions if and when the award is made.

**Applicant/Prime Institution**

Vanderbilt University Medical Center
Name of Institution

[redacted]
DUNS

Signature of Authorized Official

D. Clinton Brown, Director, Office of Sponsored Programs
Name & Title of Authorized Official

Date

**Cooperating/Subrecipient Institution**

Vanderbilt University
Name of Institution

[redacted]
DUNS

[redacted]
Signature of Authorized Official

D. Janiece Harrison, Director, Sponsored Programs Adminstration
Name & Title of Authorized Official

8/10/18
Date

Effective Date: 2/16/18

**Statement of Work**

The primary goal of this project is to evaluate the effects of Image-Guided Cochlear Implant Programming (IGCIP) techniques on basic auditory function, speech understanding, language abilities, speech production, and literacy outcomes in pediatric CI recipients. The Vanderbilt University site will be in responsible for development, maintenance, and analysis of the imaging data repository and for the creation of IGCIP plans for the 60 cochlear implant recipients that will participate in this study.

## RESOURCE SHARING PLAN

### 1. Data Sharing Plan:

Intellectual property and data generated under this project will be administered in accordance with both University and NIH policies, including the NIH Statement on Sharing Research Data (Notice: NOT-OD-03-032) issued on February 26, 2003.

We intend to publish data originating from this project in a timely manner in peer-reviewed scientific journals. Data will also be presented at national and international scientific meetings (e.g., American Auditory Society, American Speech-Language-Hearing Association, American Cochlear Implant Alliance, Society for Research in Child Development, Hearing Across the Lifespan). In addition to published papers and conference presentations, unpublished data will be discussed openly with other laboratories and investigators to encourage diversity of analysis and opinion, and to foster collaborative relationships.

We plan to provide summary updates for this project on the PIs' lab websites to help educate clinicians, outside researchers, consumers, as well as current and prospective families on the current project and findings.

The data collected for this project will be saved to our centralized data repository managed by Drs. Gifford (PI), Camarata (PI), and Dawant (Co-I). We anticipate that the de-identified database will ultimately be available and useful to all clinicians and clinician-scientists for various research-related purposes.

Data analyses and data sharing will be consistent with the NIH's commitment to promoting rigorous and transparent research (see Data Analysis, Approach, Research Strategy). To achieve transparency, details will be reported that allow other research teams to reproduce the results and raw data will be made available in tables and appendices of our publications.

### 2. Sharing Model Organisms: Not applicable

### 3. Genome Wide Association Studies (GWAS): Not applicable